06-09-03

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PTO/SB/21 (08-00)
Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/427,447
Filing Date	27 Oct 99
First Named Inventor	Alexander G. SZYNALSKI
Group Art Unit	Office of Petitions
Examiner Name	Brian HEARN
Total Number of Pages in This Submission	
Attorney Docket Number	Goen

ENCLOSURES *(check all that apply)*

- [x] Fee Transmittal Form
- [x] Fee Attached
- [ ] Amendment / Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [x] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) _____
- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to Group (*Appeal Notice, Brief, Reply Brief*)
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) *(please identify below)*:

Rule 322(a)(4) Response and Communication

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Pharmaceutical Patent Attorneys, LLC Pohl & Assoc.
Signature	
Date	See below date

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: see below date

Typed or printed name	Jacqueline SENDON		
Signature	Jacqueline Sendon	Date	06 June 03

PTO/SB/17 (10-01)
Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE

FEE TRANSMITTAL for FY 2002

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT ($) 130.00

Complete if Known	
Application Number	09/427,447
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METHOD OF PAYMENT

1. ☐ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:

Deposit Account Number

Deposit Account Name

RECEIVED JUN 11 2003 OFFICE OF PETITIONS

☐ Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17

☐ Applicant claims small entity status. See 37 CFR 1.27

2. ☑ **Payment Enclosed:**
☐ Check ☑ Credit card ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	740	201	370	Utility filing fee	0.00
106	330	206	165	Design filing fee	0.00
107	510	207	255	Plant filing fee	
108	740	208	370	Reissue filing fee	
114	160	214	80	Provisional filing fee	0.00

SUBTOTAL (1) ($) 0.00

2. EXTRA CLAIM FEES

		Extra Claims		Fee from below	Fee Paid
Total Claims	0	-20** =	0	X 9.00	= 0.00
Independent Claims	6	- 3** =	3	X 42.00	= 0.00
Multiple Dependent					= 0.00

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claim, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 0.00

***or number previously paid, if greater; For Reissues, see above*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	0.00
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	0.00
139	130	139	130	Non-English specification	0.00
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	0.00
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	0.00
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	0.00
115	110	215	55	Extension for reply within first month	0.00
116	400	216	200	Extension for reply within second month	0.00
117	920	217	460	Extension for reply within third month	0.00
118	1,440	218	720	Extension for reply within fourth month	0.00
128	1,960	228	980	Extension for reply within fifth month	0.00
119	320	219	160	Notice of Appeal	0.00
120	320	220	160	Filing a brief in support of an appeal	0.00
121	280	221	140	Request for oral hearing	0.00
138	1,510	138	1,510	Petition to institute a public use proceeding	0.00
140	110	240	55	Petition to revive - unavoidable	0.00
141	1,280	241	640	Petition to revive - unintentional	0.00
142	1,280	242	640	Utility issue fee (or reissue)	0.00
143	460	243	230	Design issue fee	0.00
144	620	244	310	Plant issue fee	0.00
122	130	122	130	Petitions to the Commissioner	130.00
123	50	123	50	Processing fee under 37 CFR 1.17(q)	0.00
126	180	126	180	Submission of Information Disclosure Stmt	0.00
581	40	581	40	Recording each patent assignment per property (times number of properties)	0.00
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	0.00
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	0.00
179	740	279	370	Request for Continued Examination (RCE)	0.00
169	900	169	900	Request for expedited examination of a design application	0.00

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid

SUBTOTAL (3) ($) 130.00

SUBMITTED BY				Complete *(if applicable)*	
Name (Print/Type)	Mark POHL	*Registration No. (Attorney/Agent)*	35,325	*Telephone*	(973) 984-0076
Signature				*Date*	6 June 03

WARNING: Information on this form may become public. Credit card information should not be included on this form. Provide credit card information and authorization on PTO-2038.

Burden Hour Statement: This form is estimated to take 0.2 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.

IN THE UNITED STATES PATENT OFFICE

Inventor	:	Alexander G. SZYNALSKI
Serial No.	:	09/427,447
Filing Date	:	27 Oct. 1999
Title	:	Stop Smoking Method & Composition
Group Art	:	Office of Petitions
Examiner	:	Brian HEARN, Senior Petitions Examiner

Commissioner of Patents
Post Office Box 1450
Mail Stop - Petitions
Alexandria, VA 22313-1450
BY EXPRESS MAIL

COMMUNICATION

Enclosed find a copy of Applicant's Rule 322(a)(4) RESPONSE and Rule 181 PETITION, together with a Fee Transmittal Form and petition fee.

Note that on the evening of June 5th, Applicant filed a Rule 322(a)(4) RESPONSE and Rule 181 PETITION by facsimile. That facsimile was sent in several parts. To assure that the Office reviews a complete and correct copy of the entire document, including all Exhibits, Applicant encloses here a replacement copy of the Rule 322(a)(4) RESPONSE and Rule 181 PETITION.

Applicant respectfully requests this complete and correct copy replace the facsimile copy previously transmitted in parts.

Respectfully submitted,

Mark Pohl, Reg. No. 35,325
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✉ *Mark.Pohl@LicensingLaw.Net*
6 June 2003

Pharmaceutical Patent Attorneys LLC
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Commissioner of Patents
Post Office Box 1450
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Alexandria, VA 22313-1450
Facsimile (703) 308-6916
BY EXPRESS MAIL

Rule 322(a)(4) RESPONSE
and
Rule 181 PETITION

This is a Rule 322(a)(4) RESPONSE to the LETTER RE CERTIFICATE OF CORRECTION mailed 6 May 2003. This is also a Rule 181 PETITION to invoke the supervisory authority of the Commissioner.

Applicant respectfully objects to the proposed Certificate of Correction. Applicant thus petitions for an order staying issue of the requested Certificate.

FACTUAL BACKGROUND

The factual record indicates that the issued claims are intended to read as printed in the issued patent. The prosecution history shows the following:

The original patent application describes a stop-smoking method. Exhibit A (A.G. Szynalski, STOP SMOKING METHOD (27 Oct. 1999)). The claims cover a three part invention. The claims as filed recite:

(A) an educational program;
(B) a hypnosis program; and
(C) lobelia.

The patent application describes lobelia, and its efficacy as an anti-smoking drug due to lobelia's antidepressant and anxiolytic activity. Thus, claim element (C), as-filed, covers lobelia literally. Under the doctrine of equivalents, claim element (C) also covered equivalent substances (*e.g.*, substances which perform the same function as lobelia, in the same way, to produce the same result).

The Patent Examiner's search revealed no prior art which suggested combining education and hypnosis with lobelia. Further, the search revealed no art suggesting combining education and hypnosis with any lobelia equivalent. Exhibit B (OFFICE ACTION (2 March 01)).

Applicant accordingly proposed changing the term "lobelia" to encompass such equivalents literally, rather than under the doctrine of equivalents. This amendment is permissible because knowledge generally available in the art need not be reiterated in the patent application itself; such information may be provided by the art. MANUAL OF PATENT EXAMINING PROCEDURE § 2164.04 (2002), *discussing* In re Wright, 999 F.2d 1557, 1562 (Fed. Cir. 1993) *and* In re Marzocci, 439 F.2d 220 (C.C.P.A. 1971). Accordingly, the "Examiner agreed to consider claims addressed to the use of anti-depressants instead of lobelia, but requested information on efficacy in this usage." Exhibit C (INTERVIEW SUMMARY (19 Sept. 2001)).

Applicant accordingly provided this information, showing that antidepressants are known to be effective anti-smoking agents. Exhibit D (AMENDMENT (19 Sept. 2001)). Applicant also requested amending the claim to replace the term "lobelia" with the term "anti-smoking drug." This amendment makes the claim cover lobelia equivalents literally, rather than under the doctrine of equivalents. The AMENDMENT, at page 5, explains:

> Element C is broadened to encompass equivalents of lobelia literally.

> The Specification teaches that lobelia is an antidepressant acetylcholine receptor binder. Specification at 13-15. The Specification teaches other examples of antidepressants, id. at 18 (gotu kola extract; kava kava root).
>
> It is known in the art that antidepressants can be used as stop smoking drugs. For example, buproprion hydrochloride is sold as both an antidepressant (commercially available under the trademark WELLBUTRIN® from Glaxo-Wellcome Inc., Chapel Hill, North Carolina) and a stop-smoking drug (commercially available under the trademark ZYBAN® from Glaxo-Wellcome Inc., Chapel Hill, North Carolina). Physicians' Desk Reference at 1277 *et seq.* (1999). Antidepressants 'produce[] a calming effect within the body, thereby relieving the stress associated with nicotine withdrawal symptoms.' Specification at 18, lines 8-9. This probably explains why individuals quitting smoking feel better when an anti-smoking drug. Id. at 15, lines 12-14.
>
> Accordingly, element (C) is broadened to encompass stop-smoking drugs generally, and dependent claims 21-24 are added to recite lobelia specifically.

Thus, the amendment doesn't necessarily change the outer limits of the claim scope, but changes the legal theory on which lobelia equivalents are covered - covering them literally, rather than under the doctrine of equivalents.

In response, the Examiner acknowledged that, as discussed in the 19 Sept. 2001 INTERVIEW SUMMARY, "[t]he term 'anti-smoking drug is broader in scope than [] lobelia." Exhibit E (OFFICE ACTION (4 Dec. 2001)).

The Examiner, however, changed position regarding whether the claim term "lobelia" may be so amended, arguing that evidence regarding knowledge in the art cannot be used to broaden literal claim coverage. Id.

The position taken in the OFFICE ACTION is contrary to law and internal Patent Office procedure. It thus precipitated another interview. The record for the ensuing interview says, "Agreed to Examiner's Amendment to place application in condition for allowance." Exhibit F (INTERVIEW SUMMARY (14 Dec. 2001)).

Regrettably, the INTERVIEW SUMMARY fails to specify exactly what amendment was agreed to.[1]

The Office then issued a NOTICE OF ALLOWABILITY. Exhibit G (NOTICE OF ALLOWABILITY (15 Jan. 03)). The NOTICE proposed an Examiner's Amendment. Id. at page 2. This amendment was proposed erroneously, because it was neither agreed to by the Applicant, nor supported by law.

Before Applicant filed an objection to the Examiner's Amendment, the Office corrected its error and withdrew the Examiner's Amendment, replacing the erroneous NOTICE with a CORRECTED NOTICE OF ALLOWABILITY. Exhibit H (CORRECTED NOTICE OF ALLOWABILITY (4 Feb. 03)). The CORRECTED NOTICE corrects the prior NOTICE, omitting the erroneous Examiner's Amendment.

The claims as issued recite "anti-smoking drug," not "lobelia." Exhibit I (U.S. Letters Patent No. 6,431,874 (13 Aug. 02)).

LEGAL ANALYSIS

Applicant respectfully believes the request for a Certificate of Correction in this case should not be granted, for several reasons. First, the records of the Patent Office do not clearly and unambiguously show the claims were printed in error; to the contrary, the record shows the Office corrected a potential error in a timely fashion. Second, the error alleged is not correctable under 35 U.S.C. § 254 as a matter of law. Third, the error alleged is not "of consequence" as is required under 35 U.S.C. § 254. We discuss each in turn.

The Patent Office Record does not clearly and unambiguously show error

An issued patent is presumed valid. 35 U.S.C. § 282. This presumption includes a presumption that the Patent Office acted correctly in reviewing and

[1] What was agreed to, was entry of an Examiner's Amendment when and if the Examiner would make of record prior art teaching the three-part combination of (A) education and (B) hypnosis and (C) a non-lobelia anti-smoking drug.

issuing the patent. *See* Superior Fireplace Co. v. Majestic Prods. Co., 270 F.3d 1358, 1381 (Fed. Cir. 2001). This statutory presumption of validity must be rebutted by clear and convincing evidence. *E.g.*, Ethicon, Inc. v. Quigg, 849 F.2d 1422 (Fed. Cir. 1988).

Here, the factual record fails to establish "clear and convincing" evidence of the alleged error. To the contrary, the record shows the claims as issued were correctly issued *vis* both the prior art of record and the papers of record. The proposed Examiner's Amendment would have violated both law and internal Office procedure, and the Office accordingly rectified this potential error.

It may be argued that the Examiner intended to include the Examiner's Amendment in the CORRECTED NOTICE OF ALLOWABILITY, but the Examiner's Amendment was omitted inadvertently. This theory fails to establish "clear and convincing" evidence of error, because it is entirely speculative, and relies on speculation regarding the Examiner's subjective intent. Evidence regarding the Examiner's intent - speculative or otherwise - cannot be relied on in proving "error." *See* Superior Fireplace Co., 270 F.3d at 1369-70 (parol evidence is generally not allowable to prove typographical or clerical error). The file itself, and the MANUAL OF PATENT EXAMINING PROCEDURE pursuant to which the file was processed, both indicate that the claims issued correctly.

It may alternatively be argued that the CORRECTED NOTICE OF ALLOWABILITY was intended to replace the original NOTICE not completely, but only partially, leaving some unspecified part of the original NOTICE (the Examiner's Amendment) in place. Assuming arguendo the CORRECTED NOTICE was intended to replace the original NOTICE only partially, it is incumbent on the Office to clearly communicate to the Applicant what part(s) of the NOTICE is intended to be changed, and what part(s) remains unchanged. I is inappropriate to conclude that the Office snuck an Examiner's Amendment into the claims by misleading the Applicant regarding the amendment status; so doing would divest Applicant of its statutory right to have the Examiner's decision reviewed by the Board of Patent Appeals.

None of these theories is supported by "clear and convincing" evidence. Here, the Office failed to clearly apprise Applicant of any intent to replace the erroneous NOTICE only in part. No continued intent to change Applicant's claims was communicated to Applicant, nor even to the Patent Office's own Publications Branch (who saw no error in the claims), nor to the Patent Office's own Office of Patent Quality Review (who saw no error in the claims). Having failed to notify Applicant (nor the other branches of the Patent Office) of its intent to enter an unauthorized amendment to Applicant's patent, the Office cannot now do so.

Issuing these claims "by mistake" would require three different PTO departments to each independently make errors

Issuing the claims in error, would require three independent Patent Office departments to have made three independent errors. First, the Patent Examiner would need to erroneously fail to include - nor even mention - the Examiner's Amendment in the CORRECTED NOTICE OF ALLOWANCE mailed to the Applicant. Second, the Patent Office Printing Branch would need to neglect to read the prosecution file and properly enter the Examiner's Amendment in the printed patent. Third, the PTO's own Office of Patent Quality Review would need to overlook the mismatch between the Examiner's Amendment and the to-be-published claims.

It is not impossible that these three independent departments of the Patent Office would each independently err. It is not impossible that these three independent errors would coincidentally pertain to the same part of the patent - the single most important part of the patent. While it is not impossible, the record fails to show "clear and convincing" evidence proving these three separate errors.

To the contrary, these alleged errors appear contradicted by the file. This is because Office procedure empowers the appropriate PTO Group to investigate the factual basis for a Certificate of Correction, and to prepare a report documenting these findings. MANUAL OF PATENT EXAM. PROC. § 1485 (2002). Here, no such report appears in the file. No report appears to have even been

requested. The Office's own failure to bother to request such a report intimates that the Patent Office believes the report would not provide any evidence to support the errors alleged.

The error alleged is not correctable under 35 U.S.C. 254

The patent statute provides a variety of procedures to correct the alleged error. A Certificate of Correction is not one of them.

The claims do not have an "immediately apparent" typographical error

The purpose of Section 254 is explained in its legislative history. In introducing the bill to the House of Representatives, Representative Lanham explained,

> The purpose of this bill is to save time and money and also promote efficiency in the operation of the Patent Office. The Patent Office is issuing approximately 40,000 patents a year. There are 15 linotype machines at the Government Printing Office engaged in doing nothing but the necessary printing for the Patent Office. Naturally, in the work at the Government Printing Office, and also in the work at the Patent Office itself, in such voluminous printing, certain *typographical errors* appear and patents are frequently issued under seal with these errors. There has been a custom prevailing in the Patent Office for 30 years, whenever these errors are detected, which are clearly clerical errors, to append a certificate of correction to the patent to show that the error was *a typographical error*, and the certificate explains this.

65 Cong. Rec. 6842-43 (1924) (emphasis added). Section 254 thus allows correction of typographical errors. Clerical or typographical errors are "generally understood to include simple mistakes such as obvious misspellings *that are immediately apparent*. Upon viewing such a misspelling, there is no doubt that a mistake, indeed a clerical or typographical mistake, has occurred." Superior Fireplace Co. v. Majestic Prods. Co., 270 F.3d 1358, 1369-70 (Fed. Cir. 2001) (italics added). An example of an error immediately apparent is an error which

"renders the claim meaningless when read literally." Sargent-Welch Scientific Co. v. J/B Industries, Inc., 496 F.Supp. 972, 978 (N.D.Ill. 1980).

Here, the mistake alleged is not "immediately apparent" on reading the claims. The claims are not "meaningless when read literally." There is no allegation that "upon reading the claims, there is no doubt that a mistake, indeed a clerical or typographical mistake, has occurred." To the contrary, the issued claims read clearly, and are fully supported by law, by the art of record and by the prosecution history. There is no allegation to the contrary.

The alleged error is not subject to a Certificate of Correction

The REQUEST FOR A CERTIFICATE OF CORRECTION alleges that the patentee has claimed more than it had a right to claim. Procedures to address this kind of alleged error are available under any of 35 U.S.C. § 135 (interferences); 35 U.S.C. § 251 (reissue), 35 U.S.C. § 302 (*ex parte* reexamination); 35 U.S.C. § 311 (*inter partes* reexamination); and 35 U.S.C. § 282(2) (anticipation of claim by prior art).

In contrast, the kind of error alleged is not correctable under 35 U.S.C. § 254. This is because alleged errors which change the scope of an issued claim cannot be corrected by a Certificate of Correction as a matter of law. This is because "Where a proposed correction involves a change in claim scope, the reissue statute is controlling, not the provisions of law governing Certificates of Correction." In re Arnott, 19 U.S.P.Q.2d 1049, 1054 (Commr. Pat. 1991), *citing* Eagle Iron Works v. McLanahan Corp., 429 F.2d 1375, 1383 (3rd Cir. 1970); *accord*, In re Shirouchi, 204 U.S.P.Q. 513 (Commr. Pat. 1979) (request to correct claims requires claim amendment beyond the scope of Certificate of Correction; the proper route to amend claims is a reissue proceeding); *see also* Superior Fireplace Co. v. Majestic Prods. Co., 270 F.3d 1358, 1375 (Fed. Cir. 2001) (as a matter of law, an alleged "mistake" that would change the scope of a claim "must thus be viewed as highly important and thus cannot be a mistake of 'minor character.'").

The Certificate of Correction requestor is well aware of the procedural safeguards mandated in interferences, reissues, *ex parte* reexamination and *inter partes* reexamination. The requestor is well aware such safeguards do not exist in reviewing a Certificate of Correction. *See* Hallmark Cards, Inc. v. Lehman, 959 F.Supp. 539, 543 (D.D.C. 1997) ("the PTO conducts a thorough and comprehensive review of a patent in reissue and reexamination proceedings" while "Certificates of Correction [] involves a far less intrusive examination of a patent for minor, typographical, and clerical errors"). The requestor attempts to have the Office shortcut required procedural safeguards, by using an inapposite procedure. Granting this request is respectfully believed beyond the Office's statutory authority.

The requestor has not alleged
any "error of consequence"

A Certificate of Correction should only be requested if the error alleged is "of consequence." MANUAL OF PATENT EXAMINING PROCEDURE § 1480 (2002). Here, it is not.

Here, the REQUEST FOR CERTIFICATE OF CORRECTION says the alleged error is "of consequence" because the patent holder is asserting the patent against the requestor. Contrary to the REQUEST FOR CERTIFICATE OF CORRECTION, asserting the patent against the requestor does not make the alleged error "of consequence." To the contrary, asserting the patent against the requestor moots the Certificate of Correction.

This is because a Certificate of Correction has effect only "on the trial of actions for causes thereafter arising," 35 U.S.C. § 254, *i.e.*, causes arising after the Certificate of Correction issues, Southwest Software, Inc. v. Harlequin Inc., 226 F.3d 1280, 1295 (Fed.Cir. 2000) (Certificate has prospective effect only). Thus, the Certificate should have no effect at all on the already-pending lawsuit. This rule is logical; if the Federal Circuit allowed Certificates of Correction to retroactively change patent claims, then every accused infringer would file a

blizzard of requests for correction, making resolution of pending infringement actions impossible.

The requestor has already been sued for infringement. The Certificate of Correction request should have no consequence on this already-pending litigation. Rather, the accused infringer's remedy for allegedly over-broad claims would be to prove in the pending litigation that the issued claims are invalid *vis* the prior art. Because the alleged error is not "of consequence" as a matter of law, the Office should accordingly deny the request. *See* MANUAL OF PATENT EXAMINING PROCEDURE § 1480 (2002).

POINT TO BE REVIEWED

Whether the Office should issue a Certificate of Correction in this case?

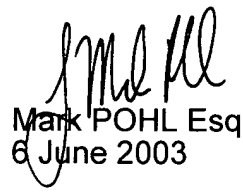
ACTION REQUESTED

Applicant respectfully believes a Certificate of Correction is not legally issuable on the existing factual record. Applicant accordingly requests that the Office deny the third-party REQUEST FOR A CERTIFICATE OF CORRECTION.

ENCLOSURES

The exhibits discussed and a Petition fee are enclosed.

Respectfully submitted,



Mark POHL Esq., Reg.No. 35,325
6 June 2003

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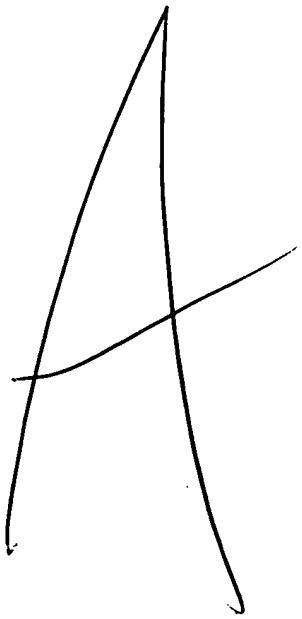


Stop Smoking Method and Composition

By Alexander Goen Szynalski

Background

The prior art discloses many stop-smoking products and methods including, for example; (A) education to educate smokers regarding smoking, its physiological dangers and addictive nature, and conscious techniques to stop smoking; (B) hypnosis, to use the unconscious mind to stop smoking; and (C) nutritional supplements, addressing the nutritional challenges with regard to stopping smoking.

Summary

While using each one of these three elements is known in the art, I have found that by combining all of these three elements together, they act on the three areas most important for stopping smoking - the conscious mind, the unconscious mind, and the body - and are synergistically effective in helping people to stop smoking.

This synergy was unexpected. I am a Certified Hypnotist and am a Nutritionist, with over twenty years experience in the fields of hypnosis, seminar presentation and nutrition. I am a member of the American Association of Professional Hypnotherapists, the National Guild of Hypnotists, the

International Association of Counselors and Therapists, and am certified by the Hypnodyne Foundation. I am listed in Who's Who in Executives and Professionals, and I was a finalist for the 1999 Ernst & Young *Entrepreneur of the Year* award. I have been a special guest on numerous national television and radio programs, and was featured on the #1 television fitness show in the country. I maintain a practice in Cedar Knolls, New Jersey. I have successfully used hypnosis in many types of situations. I have, for example, worked with athletes to improve their athletic performance, and have worked with corporations as a sales and personal-development trainer. I am driven by a sincere passion for helping people maximize their personal potential and overcome addictions to smoking and food. I enjoy a reputation for extremely high success through my seminars.

Detailed Description

My invention therefore comprises three elements: (1) education for the conscious mind regarding smoking, its physiological dangers and addictive nature, and techniques to stop smoking; (2) hypnosis for the unconscious mind, which hypnosis addresses the unconscious mind and its way of affecting behavior; and (3) dietary substances, to address the physiological needs of a person entailed in stopping smoking.

Education. The first element of my invention is education regarding smoking. This educational process can include addressing the benefits of a regular exercise program. Thus, the educational materials or program educates the smoker to engage in some form of light exercise. Not only will exercise help clear the body of the toxins acquired through smoking, but exercise will

also help release endorphins which relieve stress as well as making you feel good. Exercise will rapidly reverse the damage done to the body from smoking. If the smoker has not engaged in exercise for a long time, or the smoker has a weight problem or any other health problem, the smoker should consult their physician before starting any regimen of exercise.

In addition to this, I have found that in my preferred embodiment of my invention, the education program also addresses the physiological progression of smoking, its physiological dangers and addictive nature, and some conscious techniques to stop smoking.

The physiological progression of smoking entails three discreet steps. Knowing these steps helps the smoker recognize them as they occur, and thus recognize the needs they fill.

Stage 1 - Light a cigarette and inhale. This takes about 7 seconds. The deep breath of the inhale increases the flow of blood and oxygen to the heart and you feel more relaxed (not due to the cigarette, but due to the deep breath).

Stage 2 - Seven seconds to fifteen minutes later, nicotine enters the liver, which in turn releases sugar into the bloodstream. This results in a physical uplift (not from the cigarette, but from the release of sugar into the bloodstream) which then in turn causes the pancreas to release insulin into the bloodstream. This gives you an energy boost. Normally, it is a temporary energy boost because the muscle cells of the body are resistant to

insulin. So what happens is that your energy level goes up and then crashes, all over again. In fifteen minutes, you want to start smoking again due to the tense feelings you experience from your energy level being reduced. What we suggest is for you to sensitize your body to insulin. Before we suggest how you do this, you first should study the two diagrams pictured below. To better understand this phenomenon, we will provide an in-depth clarification of the diagrams.

Stage 3 - Fifteen to twenty minutes after beginning to smoke, the nicotine interrupts the normal transmission of neurons by competing with acetylcholine at the nerve terminal, producing such effects as an increased heart rate and respiration, along with feelings of tension and of being "wired up." It also increases arousal and a sense of well-being and focused attention. A side benefit to understanding this step is to take proper nutrients so you do not allow this physical and physiological progression of smoking to occur. This will help with maintaining or even reducing weight and increasing lean muscle tissue.

In my preferred embodiment, the smoker is educated on the physiological dangers and addictive nature of smoking. These dangers are now so widely known as to not need to be discussed in detail here.

In my preferred embodiment, the person is educated on the benefits of modifying their daily diet. This addresses

potential weight gain problems, one of the biggest fears of smokers.

Regarding potential weight gain, why do we gain weight when we stop smoking? Muscle cells become more sensitive to insulin. In my preferred embodiment, therefore, I recommend :

- Avoid refined carbohydrates. All carbohydrates start out in their rarest edible form as complex, but we make them refined by processing, preserving, storing, drying, and cooking.
- Increase physical activity, especially five to fifteen minutes after meals.
- Take 100 micrograms of chromium along with the proper cofactors, one half hour before each meal with a full glass of water. The product containing chromium (CHROMIUM CHELAVITE™) that I prefer is TRIMSPA®, available from Vitamerica, Inc., Cedar Knolls, New Jersey.
- Acquire a cigarette cessation product containing the herb lobelia, which aids any withdrawal that some may experience. Lobelia is a natural herb that tricks the body into thinking it is nicotine, but it does not have the side effects. In the preferred embodiment of my invention, I recommend CIGSATION™, available from Vitamerica, Inc., Cedar Knolls, New Jersey.
- Cut back on drinking coffee and other caffeinated beverages. Sometimes the stress or anxiety that quitters experience is due to the physiological effects of caffeine on the nervous system and not due to withdrawal from nicotine. Try drinking decaffeinated tea or some other warm decaffeinated beverage. Drinking a hot tea provides the same psychological effect as drinking hot coffee.

• Eat healthy, nourishing, non-processed foods and take a good vitamin supplement. Remember, the 200+ toxins in cigarette smoke have helped deplete the body of vitamins. Five cigarettes can deplete all the vitamin C in the body! By eating a healthy diet, you will recover your health more quickly.

In my preferred embodiment, the smoker is educated to do this for at least the first week, preferably for the first 21 days, after stopping smoking : • Eat 3 meals a day, including breakfast

• Have protein and complex carbohydrates with each meal

• Avoid sugar

• Drink 8 glasses of non-caloric liquids a day - drink water with lemon, seltzer, herbal tea, etc.

• Keep a pitcher of water on your desk and you'll easily drink 8 glasses a day

• Between meals, drink fruit juices or eat a piece of fruit

• Eat lots of fruits, vegetables and salads

• As soon as you finish eating, leave the table and go brush your teeth

• Use mouthwash whenever possible

In my preferred embodiment, the smoker is admonished : to not skip any meals (and never miss breakfast); to limit refined- sugar intake (and read packaging labels); to avoid beverages with caffeine (tea, colas, coffee, hot chocolate); and, if you must have them, drink tea or coffee out of a juice glass using a straw; and NO alcohol.

We described above the change in blood sugar levels caused by smoking and the physical and emotional response it has

on the body. If your blood sugar level gets low, you will either crave a cigarette or something sweet. In either case, it will boost your blood sugar level for 10 to 20 minutes and then cause a crash, triggering another urge for a cigarette or a sweet. By eating 3 meals a day, you will tend to have a stable blood sugar level, and this minimizes cigarette and eating urges. Eating protein with carbohydrates at breakfast sets the stage for stable blood sugar levels all through the day. Protein with complex carbohydrates stabilizes the blood sugar.

I have also found it useful to teach persons quitting smoking to carry a nonfood item such as a swizzle stick or a low calorie food such as celery or carrot sticks. Use these to gratify any oral habit that has been developed by the conditioned response of putting your hand to your mouth 250 times a day, as if you were a one pack a day smoker.

By providing the smoker with this kind of educational program, the smoker is able to consciously and analytically understand their need to smoke and to approach the decision to smoke, or to not smoke, in an analytical, dispassionate manner.

Hypnosis. In addition to the conscious, analytical mind, one can aid the stop-smoking process by using the subconscious mind. In my invention, it is important to use both the conscious mind - via the educational program discussed above - and the unconscious mind, with hypnosis.

The subconscious mind dominates your thinking and behaviors. It is programmed using repetition and the subconscious mind basically behaves for two reasons. It tries to take you towards pleasure and it wants you to stay away from pain. For

example, when you have a cup of coffee, you grab a cigarette; you get into a car, you grab a cigarette; you get stuck at a light, you grab a cigarette; you get a break at work, you grab a cigarette; you have a cocktail, you grab a cigarette. If you do not experience these triggers, you may very often go many hours without having a cigarette. It is important that you identify these scenes so we can then break the connection of the cigarettes to the scenes.

With hypnosis, the subconscious mind no longer aids the body to smoke more often, but rather aids the body to stop smoking, during precisely those periods when a smoker is accustomed to having a cigarette. Instead of the subconscious making the body scream for nicotine after a meal, or with coffee or alcohol, the subconscious will help the smoker remain calm and pain free.

When used to stop smoking, I have found that in my preferred embodiment, the hypnosis focuses on interrupting "conditioned responses" generally, and specifically, on interrupting the response to smoke. Conditioned responses are actions (e.g., reaching for a cigarette) motivated not by a consciously-perceived need, but rather by unconscious habit.

Is smoking more of a physical or more of a psychological addiction? For example, how many times have you gone two, three or four hours without even smoking one cigarette and then in another hour you may smoke four, five or six cigarettes? Why is that? It is because certain events, or certain times of the day can trigger you to smoke a cigarette. Therefore, it is necessary

to break these unconscious connections, and such breakage occurs, I found, most efficiently using unconscious means - hypnosis.

In my preferred embodiment of my invention, the hypnosis is done in-person and is reinforced later with prerecorded media such as audio-tapes.

Hypnosis techniques are known in the art. In my preferred embodiment, I prefer the in-person hypnosis to follow a six-step protocol. The six steps are (1) neuro-linguistic programming, (2) physical positioning, (3) progressive relaxation, (4) occupying the critical/analytical factor, (5) a process of suggestion, and (6) changing the language of the subconscious.

(1) Neuro-linguistic programming is a technique known in the art. It is described in detail in the following works written since the 1960's.

The Structure of Magic, Vol.1 - Richard Bandler/John Grinder

The Structure of Magic, Vol.2 - Grinder/Bandler

Patterns of Hypnotic Techniques of M.H. Erickson, Vol.1 - Bandler/Grinder

Patterns of Hypnotic Techniques of M.H. Erickson, Vol.2 - Grinder/Bandler

Frogs Into Princes - Bandler/Grinder

Tranceformations - Grinder/Bandler

Using Your Brain for a Change - Richard Bandler

Time for a Change - Richard Bandler

Persuasion Engineering - Richard Bandler/John La Valle

The Adventures of Anybody - Richard Bandler

Science and Sanity - Alfred Korzybski

Uncommon Therapy - The Psychiatric Techniques of Erickson - Jay Haley

Training Trances - John Overdurf / Julie Silverthorn

My Voice Will Go With You - Sidney Rosen

These are incorporated herein by reference.

(2) Physical positioning is important, to maintain the subject in a state which is both relaxed, yet not sleep-prone.

(3) Physical Positioning and Progressive Relaxation follow the methods known in the art, instructing the subject to progressively relax each part of their body. This can be done with instructions to, for example, physically perform some act, or to mentally visualize some relaxing phenomenon.

(4) Occupying the critical / analytical factor is accomplished in my preferred embodiment by having the subject perform certain tasks which both require some conscious attention, but also are not so difficult or complex as to absorb the subject's entire mental capacity.

(5) The process of suggestion is important to repeat for an effective period of time - usually at least daily for about twenty one days. This time may, however, be less when the subject is relaxed, or is in a highly-emotional state.

(6) The last step is changing the language of the subconscious. This is done by repeating a desired message - *e.g.*, "I am free from smoking" - often enough that the desired message replaces an undesired message in the subconscious mind. For example, one technique is to get friends, coworkers, and family members to help you, by asking them to congratulate you for not smoking. The best way to accomplish this is to stick your hand

out to a friend or family member, asking that person to shake your hand and congratulate you for being a nonsmoker. When that person congratulates you, it is a positive reinforcement. The (former) smoker benefits from this positive feedback, and from knowing that they are doing well in stopping smoking.

In another technique I found successful, smoking is described as like having a best friend. Psychologically, the cigarette is the support that a friend gives you. Imagine having your best friend there for you and then losing him or her. You would not feel very good losing your best friend. However, if you discover that your best friend was abusing your children, most likely you would not feel the same about losing your best friend. You would still have some sort of attachment, but now you would be able to reason your way out of not having this person as a friend. In my preferred embodiment, the educational program teaches smokers to look at smoking in the same way.

In my preferred embodiment of my invention, hypnosis is also administered by listening to a prerecorded audio script which provides stop-smoking messages and positive feedback for not smoking. Such audio tapes are commercially available. In my preferred embodiment, I use an audio tape titled "Smoking Cessation," published by Vitamerica, Inc., Cedar Knolls, New Jersey, www.vitamerica.com, to be listened to once every day for an effective length of time, generally about twenty-one days.

Dietary Substances. The third element of my invention is using proper dietary substances. These address the physiological needs of people breaking their physical addiction to

nicotine. Further, one of the biggest fears of smokers is that, in stopping smoking, they will gain excess weight. Thus, in my preferred embodiment, in addition to the dietary substances that support normal form and function while recovering from a smoking addiction, one also uses dietary substances that support normal form and function for those seeking weight-loss or to reduce weight gain. In my preferred embodiment, I recommend CIGSATION™ and TRIM SPECIFICS™, dietary supplements by Vitamerica, Inc., Cedar Knolls, New Jersey, www.vitamerica.com

To aid the reader's understanding, I will discuss first the biological basis of the smoking addiction. I will then discuss the dietary substances and the diet modifications I have found effective to combat the physical smoking addiction - the addiction to nicotine. Finally, I will discuss dietary substances to control weight gain.

What causes the addiction to nicotine? The nervous system is divided into two anatomical divisions. The first is the central nervous system, which is composed of the brain and spinal cord. The second is the peripheral nervous system, which includes neurons located outside the brain and spinal cord, which includes any nerves that enter or leave the central nervous system. The peripheral nervous system can be further divided into the efferent division, whose neurons carry signals away from the brain and spinal cord to the peripheral tissues, and the afferent division, whose neurons bring information from the periphery to the central nervous system.

Nerve impulses are transmitted along a path of cells called neurons. The neurons form a knot-like mass called ganglia.

These neurons are connected by a series of bridges. The bridge is called a synapse. In order to cross the bridge, a neurotransmitter is required. Before the nerve impulses reach the relay station or bridge, they are referred to a pre-ganglionic neurons. After crossing the synapse, they are referred to as post-ganglionic neurons. The basic neurotransmitters of the autonomic nervous system are acetylcholine and epinephrine. Acetylcholine mediates the transmission of nerve impulses across autonomic ganglia in both the sympathetic and parasympathetic nervous systems.

Nicotine Receptors. These receptors, in addition to binding acetylcholine, also recognize nicotine. Nicotine initially stimulates and then blocks the receptor. There is a competitive inhibition taking place. In lay terms, the receptor has a greater affinity for nicotine than for acetylcholine. At the same time, nicotine increases the level of the neurotransmitter dopamine in a particular brain pathway which associates a molecular link between nicotine addiction and this pleasure producing pathway. This is why nicotine causes such as strong physiological addiction. Recently, scientists at Yale and at the Pasteur Institute in Paris have found that the beta 2 sub unit of a known nicotine receptor in the brain is a critical component in nicotine addiction.

To combat this nicotine addiction, it is useful to use lobelia. *Lobelia inflata* (also known as Indian Tobacco) is a plant. This plant contains three nicotine-like ingredients : 1) lobeline, 2) lobelanidine, and 3) lobelanine. On close inspection of these three ingredients one can notice that all are symmetrical

molecules. In other words, if you cut them each in half, each half is the same. The only exception is with lobeline, which has a slight difference on one side of the molecule. I refer to each of these three compounds, their analogs, and derivatives, as "lobelia." After explaining some basic physiology, you will see why lobelia is important.

Nicotine causes an increase in blood pressure, increases intestinal motility, stimulates the central nervous system, has an anti diuretic effect (ability to retain water), affects heart rate, affects respiration, is highly soluble and crosses the blood-brain barrier, produces some euphoria (feeling of well being), arousal, relaxation, and it improves attention, and crosses the placenta membrane and is secreted in the milk of lactating women.

The chronic effects of Nicotine include nasopharyngeal and bronchial irritation, lung cancer, cardiac irregularities, stimulated salivary secretion, and reduction of gastric acidity.

Let us now consider the structural formulas for the active constituents in lobelia. Because of their basically symmetrical structure, it appears that they have an advantage in competing with nicotine at the effector cell site. It is postulated that these components can attach themselves to the cell site from either side of the molecule and perhaps crowd out the nicotine. Later, after the nicotine is eliminated from the system, lobeline will replace nicotine at the effector cell site. While nicotine is rapidly eliminated from the body within 16-24 hours, the withdrawal symptoms can last for several weeks to several months, depending upon the individual.

Lobelia's action in the body mimics that of nicotine, but does not have the physiological dependence of nicotine. Lobelia exhibits a cross tolerance with nicotine, is one of the most useful systemic relaxants, has a relaxation effect on the central nervous system, has a relaxing action on the autonomic nervous system, has a general relaxing action on neuromuscular action, is a powerful respiratory stimulant, equalizes circulation and relieves vascular tension, provides a truly holistic action with a combination of stimulation and relaxation, and also provides the holistic action of a general relaxant with diffusive stimulation.

Recently, scientists in Japan have discovered an antidepressant component in the leaves of *lobelia inflata*. This probably explains why individuals feel better when taking lobelia.

Given this physiology, the physiologic needs of a smoker can be addressed using lobelia. In addition to lobelia, I have found that other herbal substances are useful as dietary substances. Thus, in my preferred embodiment, lobelia is used along with wood betony, fennel seed and licorice root and several other herbs.

In addition to these vitamin-type nutritional supplements, in my invention one needs lobelia. Lobelia is also known as Indian tobacco or wild tobacco and is native to North America. It includes three components significant here : lobeline, lobelanidine and lobelanine. It is pharmacologically similar to nicotine, but does not have nicotine's physiological dependency.

In my preferred embodiment of my invention, I have found it beneficial to include certain other supplements derived from

plants and herbs. Each the individual ingredients improves the function of lobelia alone, as each provides a specific function to enhance the efficacy of the product.

Wood Betony. Wood betony is used for its sedative and bitter properties. Its anti-hypertensive properties relieve nervous tension and dilate blood vessels, thus producing a calming effect. Wood betony can relieve headaches normally associated with nicotine withdrawal. Its bitter tonic properties also aid in nicotine withdrawal.

Fennel Seed. Fennel seed has been recognized to have carminative and stimulant properties. It has been reported to have a spasmolytic effect on smooth muscles. As a result, it can be used for dyspeptic discomfort, gastrointestinal discomforts and congestion of the upper respiratory tract. Since chain smokers normally have a smoker's cough resulting in congestion of the lungs, fennel seed can aid in treating that congestion. One of the constituents from the volatile oil expressed from fennel is anethol. Anethol has been shown experimentally to reduce secretions of the upper respiratory tract (i.e., lungs).

Licorice Root. The major active ingredient in licorice root is glycyrrhizin. The glycyrrhizin is responsible for a vasopressor response, which is similar to that occurring in nicotine. However, while it mimics that response, it also exhibits anti-inflammatory and an antitussive effects that is comparable to codeine in potency. This is due to the derivative 18 Beta-glycyrrhetinic acid which prevents smoker's cough. In addition, the flavonoids in licorice root have recently been shown to have strong antioxidant and anti-hepatotoxic activities. These

activities will help cleanse the body of the free radicals and other toxic substances generated from smoking. Licorice extracts are often used in anti-smoking preparations as a flavoring agent to mask bitter nauseous or other undesirable tastes from other components of the preparation. Licorice can also be used to treat stomach irritation arising from nicotine usage.

In addition to the foregoing, I have found it useful to use also blue cohosh, black walnut husk, chamomile flower, gotu kola leaf extract, kava kava root, peppermint, sarsaparilla root, slippery elm bark, valerian root, bayberry fruit, myrrh, passion flower, ginger root and eucalyptus oil. Thus, in my preferred embodiment, I use each of these, for the following reasons.

Blue Cohosh. It has demonstrated anti-inflammatory activity in animals. Blue cohosh can be used for nervous disorders.

Black Walnut Husk. Black walnut husk is a blood cleanser and oxidizer. It has been shown to be useful in lung disease and has strong anti-fungal and antibacterial properties. It is a rich dietary source of protein, iodine, chromium, potassium, manganese, vitamin A and the powerful antioxidant vitamin C.

Chamomile Flower. Chamomile flower has essential oils that contain a variety of glycosides, and other important constituents and chemically related compounds. Several of the therapeutic constituents of the volatile oil are chamazulene and alpha bisabolol oxide A. Chamazulene has demonstrated anti-inflammatory activity, pain relieving, wound healing, antispasmodic and anti-microbial properties. Alpha bisabolol has

anti-inflammatory, anti-microbial and anti-peptic activities. Matricin has been found to have a sufficiently stronger anti-inflammatory effect than chamazulene.

Gotu Kola Leaf Extract. The gotu kola leaves contain properties that have been shown to accelerate wound healing, improve memory, relieve fatigue and stress, increase mental acuity and improve behavioral patterns. This produces a calming effect within the body, thereby relieving the stress associated with nicotine withdrawal symptoms.

Kava Kava Root. The active ingredients in kava kava root are a group of compounds known as the kavalactones. They are recognized for their biological activity as a sedative, anti-convulsive and tonic. Additional constituents in kava kava root have demonstrated muscle relaxant activity and have been used for their ability to combat nervous anxiety and unrest. Kava kava also has expectorant properties. This allows the heavy smoker to expectorate residual mucus from the lungs.

Peppermint. Peppermint yields a volatile oil that is composed mainly of menthol. Menthol has long been recognized as a cooling agent in topical preparations. Also present are many other ingredients, some of which have been characterized to have biological activity. One such constituent is bisabolene, which has demonstrated to have anti-inflammatory activity. Other constituents in peppermint include flavonoids such as hesperetin and rutin. Also present are tocopherols, carotenoids, choline and azulenes. Azulene isolated from peppermint demonstrated anti-inflammatory and antinuclear effects in experimental animals. Peppermint oil is extensively used as a flavoring agent,

carminative, antiseptic and local anesthetic in cold, cough and other preparations. Peppermint and their oils have been used in traditional medicine as a stomachic, stimulant, antiseptic, local anesthetic and antispasmodic in treating indigestion, sore throat, nausea, diarrhea and colds.

Sarsaparilla Root. The major component of sarsaparilla is a variety of steroids which include sarsasapogenin, smilagenin, sitosterol, stigmasterol and pollinastanol, and their glycosides (saponins) including sarsasaponin (parillin), smilasaponin (smilacin), sarsaparilloside and sitosterol glucoside. Sarsaparilla is reported to have hepatoprotective, diuretic and anti-inflammatory activity.

Slippery Elm Bark. The principal constituent of slippery elm bark is mucilage. The mucilage has demulcent (soothing) and nutritive properties. It can sometimes be used to soothe irritated lungs.

Valerian Root. Valerian root has a variety of constituents but the major one, valerenic acid, produces a nerving or sedative effect. Valerian has CNS depressant activities. As a result, in states of agitation normally witnessed by smokers during withdrawal, this will have a calming effect. It has also been shown that in conditions of fatigue, the herb has demonstrated stimulating properties.

Bayberry Fruit. Bayberry fruit has been recognized to have a tonic effect.

Myrrh. Myrrh is reported to have astringent effects on mucus membranes. It is often used as a flavor component to mask bitter ingredients. It has also been used as a stimulant and

expectorant. The expectorant properties will help the smoker remove mucus and phlegm from the lungs.

Passion Flower. Passion flower contains indole alkaloids, flavonoids and steroids. The indole alkaloids and flavonoids have tranquilizing effects. Anxiolytic and hypotensive activity has also been reported.

Ginger Root. Ginger root is used to combat nausea and vomiting, which may accompany nicotine withdrawal.

Eucalyptus Leaf Oil. The leaves contain .05 to 3.5% oil. The oil consists mostly of eucalyptol (1, 8-cineole). It is used in an anti-smoking formula as an expectorant to help remove mucus from the lungs.

In my preferred embodiment of my invention, these dietary substances are used as found in CIGSATION™ 100% Natural Cigarette Replacement System, commercially available from Vitamerica, Inc., Cedar Knolls, New Jersey 07927, www.vitamerica.com. Each of these dietary substances adds to the benefit obtained from using lobelia alone.

In addition to addressing the physical nicotine addiction, I find it useful to address the smoker's fear of excessive weight gain, by using a "weight control product," a drug or dietary substances useful in controlling unnatural weight gain. Such dietary substances include chromium, choline, inositol, vanadium, gynema sylvestre, lecithin, vitamin B6, ginseng, zinc, mahuang, kola nut extract, spirulina, and methionine. Several of these are known physiological stimulants, which increase thermogenesis in the body and thus promote expending calories. I

will discuss each in turn, and its usefulness in a weight-control product.

Chromium. What is chromium? It's the mineral that no body can afford to be without. Like iron, copper and zinc, chromium is one of the 16 essential trace minerals the body needs to keep healthy and fit. And for people who are overweight and out of shape, chromium may be the most precious mineral of all. In its biologically active form, it helps insulin to metabolize fat, convert protein into muscle, and convert sugar into energy. Chromium-activated insulin actually increases almost twenty times the amount of glucose available for energy production, optimizing energy output so that you feel healthy and alive.

Chromium is the "master" nutrient for controlling blood sugar. It helps overcome sugar cravings, which is a problem with many overweight people. It also plays an important role in controlling blood lipids, lowering harmful LDL cholesterol, and increasing beneficial HDL cholesterol.

Research shows that a chromium deficiency may be a widespread problem. Many people, such as athletes, diabetics, mothers and the elderly, are at especially high risk. A lack of chromium can impair insulin function, thereby inhibiting protein synthesis and energy production. More seriously, it can even lead to type II diabetes and heart disease.

In my preferred embodiment, the chromium is a form of chromium commercially available under the trade name CHROMIUM CHELAVITE™, available from Vitamerica, Inc. of Cedar Knolls, New Jersey.

The most biologically active form of chromium, the true GTF chromium, is the basis for the molecular structure of CHROMIUM CHELAVITE™. Studies on CHROMIUM CHELAVITE™ at a leading Utah university have shown that this form of chromium is clearly superior to both chromium picolinate and chromium polynicotinate in absorb ability. It had an absorption rate that was 53% greater than for chromium picolinate and 91% greater than that observed for chromium polynicotinate.

Choline. Choline is one of the most beneficial nutritional supplements. Technically, it is not a vitamin, even though it is essential for human life. There are three major functions of choline among humans. It is needed for building cell structure, it prevents or minimizes unhealthy fat deposits in the liver, and it acts as a precursor to acetylcholine. Acetylcholine is a neurotransmitter in the brain which is responsible for nerve impulses, memory, learning, mood elevation and depression control.

Choline has a very positive effect on the health of the liver. It is a lipotropic agent (fat eliminator) that can cut away fats in the liver to be used instead of energy. Choline aids in weight loss by facilitating Growth Hormone (GH) releasers, controlling cholesterol, and helping control the appetite. It also helps reduce the "gut transit time", the amount of time it takes food to move through the intestines. In addition to helping speed food through the system, choline also plays an important role in the body's ability to metabolize fat and cholesterol.

Inositol. Inositol is a member of the B complex of vitamins. It provides a calming effect, nourishes brain cells, helps reduce cholesterol, slows artery hardening, prevents eczema,

and is needed for hair growth and metabolism. It is found in high concentrations in the brain, and serves as a brain cell membrane stabilizer. Inositol also helps in lecithin formation, and aids the body in the metabolism of fat and cholesterol.

Vanadium. A trace mineral like chromium, vanadium is essential for cellular activity and for the formation of bones and teeth. It also inhibits the synthesis of cholesterol and lowers certain forms of high blood pressure. It works remarkably well as a powerful insulin mimic and has been shown to normalize blood sugar levels, even in diabetics.

Gynema Sylvestre. This tropical herb is beginning to receive much attention due to impressive results in recent studies. Gynema Sylvestre appears to have a positive effect in lowering blood sugar levels, especially in diabetics. Research also suggests that it can help curb sugar absorption.

Lecithin. Lecithin is part of every single cell in the body, but has its greatest concentration in the brain. About 17-20% of the brain is made up from lecithin. Lecithin is an emulsifier. It is used in the manufacture of chocolate, because it keeps it liquid and it keeps it moving. Lecithin does the same thing for the fat in the human body; it keeps it moving, right out of the body.

Lecithin is a natural diuretic and an effective cholesterol reducer. It helps prevent the buildup of cholesterol on arterial walls, thus improving the circulation of the blood. One study that examined 900 men for atherosclerosis (fat deposits in the arteries) showed that those with more than 36% lecithin in

the blood had no atherosclerosis. Those with less than 34% showed evidence of the disease.

Lecithin is also the source of two of the hardest to find B-Complex relatives, choline and inositol. A major function of lecithin is to supply choline in the diet. Choline (see entry) has the function of breaking down fat deposits in the body. Our bodies do not manufacture enough choline. Therefore, we must rely upon our food and supplements such as lecithin to make sure that we get enough.

Vitamin B6. Vitamin B6 aids in more bodily functions than any other single nutrient. It facilitates the body's use of carbohydrates, proteins and fats. It promotes mental performance by aiding in the transport of amino acids, which are used by the brain to increase mental energy and memory. It also promotes the transport of choline, and aids in the breakdown of glycogen, the primary fuel for the brain.

Ginseng. For centuries, the Chinese have testified to the beneficial effects of Ginseng on longevity. Ginseng provides stimulation to the entire body, helping to overcome stress and fatigue. Ginseng can regulate and normalize blood pressure and blood sugar levels. It has been called a cure-all and has also been claimed to be a mild sexual stimulant. Over all, Ginseng has a phenomenal effect on the body's energy level.

Zinc. Zinc is another important trace mineral that is used by more than 200 enzymes to keep the body's major metabolic systems going strong. In addition to its role in metabolism, zinc is a potent antioxidant, profoundly important in enhancing the

immune system, stimulating cellular growth, reducing excess levels of damaging free radicals, and improving general health.

Mahuang. Mahuang, also known as ephedra, contains a potent alkaloid, ephedrine. This natural stimulant increases the basal metabolic rate, which helps to burn calories more effectively. It has also been used as a remedy for kidney and bladder problems, as well as for colds, asthma, and hay fever.

Kola Nut Extract. This is a natural stimulant that increases energy and stamina. It has been found to be very useful in preventing fatigue. Kola Nut Extract also acts as a tonic agent for the heart, and it is sometimes useful in relieving pain, neuralgia, and headache.

Spirulina. This famed blue-green algae contains concentrations of nutrients unlike any other single grain, plant or herb. This super nutrient is a naturally digestible food that aids in protecting the immune system, in cholesterol reduction and in mineral absorption. It also helps to cleanse and heal, while also curbing the appetite.

Methionine. Methionine is an amino acid that assists the gall bladder function by helping to synthesize bile salts. It is a lipotropic substance that prevents the deposits of and cohesion of fats in the liver. It is also reported to be a growth hormone releaser.

It serves as an antioxidant in the brain. It helps prevent the buildup of heavy metals and plays an important and essential role in the production of the brain neurotransmitter choline. Methionine is not found in the body. Therefore, it must be gotten via food and supplementation. It is also a good source

of sulfur, and its therapeutic lipotropic effects help to eliminate fatty substances from the body.

Each of these dietary substances can be found in TRIM SPECIFICS™, available from Vitamerica, Cedar Knolls, New Jersey, www.vitamerica.com.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to is fullest extent. The examples I discuss here are included as the preferred embodiment of my invention, and not to further qualify the description.

Claims

I claim:

1. A method for helping a tobacco smoker to stop smoking, said method comprising the steps of:

(A) providing to a tobacco smoker an educational program to educate said tobacco smoker's conscious mind, said educational program including education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) providing to said tobacco smoker at least one hypnosis program to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) providing to said tobacco smoker lobelia in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco,

such that said tobacco smoker can be helped to stop smoking.

2. The method of claim 1, further comprising the step of: (D) providing to said tobacco smoker, wood betony.

3. The method of claim 2, further comprising : (E) providing to said tobacco smoker, fennel seed.

4. The method of claim 3, further comprising the step of: (F) providing to said tobacco smoker, licorice root.

5. The method of claim 4, further comprising the step of: (G) providing to said tobacco smoker, black walnut husk, chamomile, kava kava root, peppermint, sarsaparilla root, valerian root, bayberry root, passion flower, ginger root, eucalyptus leaf oil, lecithin, vitamin B6, ginseng, zinc, spirulina, and methionine.

6. The method of claim 1, where said hypnosis program comprises prerecorded media useable by said tobacco smoker when alone.

7. The method of claim 1, further comprising the step of: (D) providing to said tobacco smoker, at least one weight-control product.

8. The method of claim 7, where the weight control product includes at least one stimulant.

9. The method of claim 8, where the stimulant is selected from the group consisting of mahuang, kola nut extract, gotu kola leaf extract and myrrh.

10. The method of claim 9, wherein the weight control product comprises chromium.

11. A product to aid a tobacco-smoker in ceasing to smoke tobacco, said product comprising:

(A) means for educating said tobacco smoker's conscious mind, said educational program including education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) means for hypnosis to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) lobelia in an amount effective to aid in the reduction or cessation of said smoker's craving to smoke tobacco.

12. The product of claim 11, further comprising: (D) wood betony.

13. The product of claim 12, further comprising: (E) fennel seed.

14. The product of claim 13, further comprising: (F) licorice root.

15. The product of claim 14, further comprising: (G) black walnut husk, chamomile, kava kava root, peppermint, sarsaparilla root, valerian root, bayberry root, passion flower, ginger root, eucalyptus leaf oil, lecithin, vitamin B6, ginseng, zinc, spirulina, and methionine.

16. The product of claim 11, where said means for hypnosis comprises prerecorded media useable by said tobacco smoker when alone.

17. The product of claim 11, further comprising: (D) at least one weight-control product.

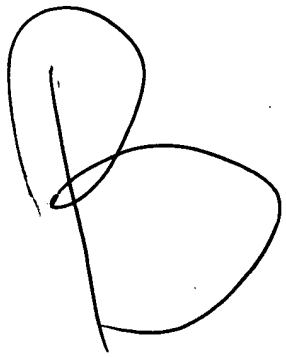
18. The product of claim 17, where the weight control product includes at least one stimulant.

19. The method of claim 18, where the stimulant is selected from the group consisting of mahuang, kola nut extract, gotu kola leaf extract and myrrh.

20. The method of claim 19, wherein the weight control product comprises chromium.

Abstract of the Disclosure

The inventor discloses a unique, new and useful process to reduce tobacco smoking, entitled Stop Smoking Method and Composition, consisting of: (1) educating tobacco smokers regarding smoking, its physiological dangers and addictive nature, and techniques to stop smoking; (2) hypnotizing said tobacco smokers, and (3) providing dietary substances to address the nutritional needs of nicotine addiction and the nutritional challenges thereof.



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/437,447	10/27/99	SZYNALSKI	A

EXAMINER	
RIMELL, S	
ART UNIT	**PAPER NUMBER**
3712	2

DATE MAILED: 03/02/00

QM32/0302

MARK POHL
55 MADISON AVENUE 4TH FLOOR
MORRISTOWN NJ 07960

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/427,447	SZYNALSKI, ALEXANDER GOEN	
	Examiner	Art Unit	
	Sam Rimell	3712	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

14) ☒ Notice of References Cited (PTO-892)
15) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
16) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
17) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
18) ☐ Notice of Informal Patent Application (PTO-152)
19) ☐ Other:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1 and 11 set forth a method in which lobelia is used "in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco." However, the disclosure does not reveal what this amount actually is. In fact, the disclosure does not reveal the therapeutically effective dosage amounts for any of the substances disclosed, so the specification is non-enabling for all of claims 1-20. Simply making reference to an OTC product, such as "Cigsation" or "Trim Specifics" is insufficient to meet the disclosure requirement since OTC products do not always label the dosages or contents of the of the substances they contain.

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-20 are rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility.

Claims 1-20 are a claimed method in which he craving to smoke is alleged to be reduced or ceased by the use of education materials, hypnopsis, and the ingestion of naturally occurring

substances, such as lobelia. Additional substances, such as wood betony, licorice root, and peppermint are also alleged as being therapeutically effective. However, there is no evidence that the combined use of educational materials, hypnosis, and the recited natural substances produces a therapeutically effective method for reducing or eliminating a craving for smoking. There is no clinical evidence that the combined effects will produce the claimed result. In addition, the reference to Schneider et al. (US Pat. 5,414,005) contains a statement in column 3, lines 5-9 that orally ingested lobeline has never been shown to be therapeutically effective in reducing a craving for smoking. Since the other required steps of providing educational materials and providing hypnosis have also never been shown to be therapeutically effective, there is no reason to assume that the combined usage of educational materials, hypnosis and lobeline will be therapeutically effective.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-20 are rejected under 35 U.S.C. 102(b) as being anticipated by admitted prior art to Vitamerica Inc .

Applicant's disclosure admits (page 5, para 4) that lobeline is utilized in a known prior art ingestible product known as "Cigsation". Applicant's disclosure (page 26, para 2) admits that all the remaining claimed substances are contained in a known prior art ingestible product called "Trim Specifics". Applicant's disclosure further admits (page 11, para 4) that the hypnosis and

education steps are contained in a known prior art tape program called "Smoking Cessation". All of these products are available from a common source, known as Vitamerica Inc., and are availalble on the internet at www.vitamerica.com. Since each of these products derives from a common source, it is reasonable to presume that they are intended to be used together in a method for addressing a smoking addiction.

Any inquiry concerning this communication should be directed to Sam Rimell at telephone number (703) 306-5626.

Sam Rimell
Primary Examiner
Art Unit 3712

Notice of References Cited	Application/Control No. 09/427,447	Applicant(s)/Patent Under Reexamination SZYNALSKI, ALEXANDER GOEN	
	Examiner Sam Rimell	Art Unit 3712	Page 1 of 1

U.S. PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	NAME	CLASS	SUBCLASS	DOCUMENT SOURCE ** APS	OTHER
☐	A	5414005	May. 1995	Schneider et al.	514	343	☐	☐
☐	B	5780051	Jul. 1998	Eswara et al.	424	449	☐	☐
☐	C	5965567	Oct. 1999	Archer et al.	514	282	☐	☐
☐	D						☐	☐
☐	E						☐	☐
☐	F						☐	☐
☐	G						☐	☐
☐	H						☐	☐
☐	I						☐	☐
☐	J						☐	☐
☐	K						☐	☐
☐	L						☐	☐
☐	M						☐	☐

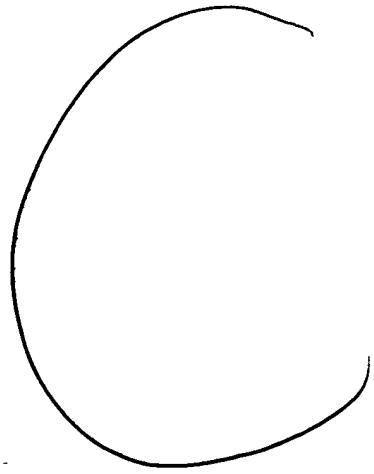
FOREIGN PATENT DOCUMENTS

*		DOCUMENT NO.	DATE	COUNTRY	NAME	CLASS	SUBCLASS	DOCUMENT SOURCE ** APS	OTHER
☐	N							☐	☐
☐	O							☐	☐
☐	P							☐	☐
☐	Q							☐	☐
☐	R							☐	☐
☐	S							☐	☐
☐	T							☐	☐

NON-PATENT DOCUMENTS

*		DOCUMENT (Including Author, Title Date, Source, and Pertinent Pages)	DOCUMENT SOURCE ** APS	OTHER
☐	U		☐	☐
☐	V		☐	☐
☐	W		☐	☐
☐	X		☐	☐

*A copy of this reference is not being furnished with this Office action. (See Manual of Patent Examining Procedure, Section 707.05(a).)
**APS encompasses any electronic search i.e. text, image, and Commercial Databases.



UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/427,447	10/27/99	SZYNALSKI	A

EXAMINER	
RIMELL, S	
ART UNIT	**PAPER NUMBER**
2166	16

TM02/0920

MARK POHL
55 MADISON AVENUE, 4TH FLOOR
MORRISTOWN NJ 07960

DATE MAILED: 09/20/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Interview Summary	Application No.	Applicant(s)	
	09/427,447	SZYNALSKI, ALEXANDER GOEN	
	Examiner	Art Unit	
	Sam Rimell	2166	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Sam Rimell*. (3)_____.

(2) *Mark Pohl*. (4)_____.

Date of Interview: *19 September 2001* .

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☒ No.
If Yes, brief description: _____ .

Claim(s) discussed: *1 and 11* .

Identification of prior art discussed: *Cooper et al.* .

Agreement with respect to the claims f)☐ was reached. g)☐ was not reached. h)☒ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Examiner suggested modifying claims 1 and 11 to define non-invasive educational techniques, unlike those of Cooper et al. which are invasive to the body. Examiner agreed to consider claims addressed to the use of anti-depressants instead of lobelia, but requested information on efficacy in this usage* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

i)☐ It is not necessary for applicant to provide a separate record of the substance of the interview(if box is checked).

Unless the paragraph above has been checked, THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check the appropriate box at the bottom of the Form which informs the applicant that the submission of a separate record of the substance of the interview as a supplement to the Form is not required.

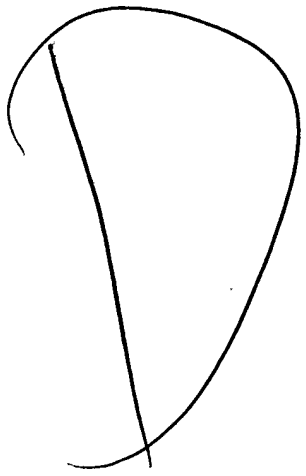
It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.



Please type a plus sign (+) inside this box → ☐

PTO/SB/21 (08-00)
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U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/427,447
Filing Date	27 Oct 1999
First Named Inventor	Alexander Goen SZYNALSKI
Group Art Unit	2166
Examiner Name	Samuel RIMELL, Esq.
Total Number of Pages in This Submission	
Attorney Docket Number	Nutrimerica

ENCLOSURES *(check all that apply)*

- ☑ Fee Transmittal Form
  - ☑ Fee Attached
- ☑ Amendment / Reply
  - ☐ After Final
  - ☑ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Response to Missing Parts/ Incomplete Application
  - ☐ Response to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Assignment Papers *(for an Application)*
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) one
- ☐ After Allowance Communication to Group
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- ☐ Proprietary Information
- ☐ Status Letter
- ☐ Other Enclosure(s) *(please identify below)*:

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual name	Mark POHL, Reg.35,325, Pharma. Patent Attys
Signature	
Date	See below date

CERTIFICATE OF MAILING

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, DC 20231 on this date: see below date

Typed or printed name	Mark POHL, Reg. No. 35,325		
Signature		Date	19 Sept 01

PTO/SB/17 (11-00)
Approved for use through 10/31/2002. OMB 0651-0032
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it displays a valid OMB control number.

FEE TRANSMITTAL for FY 2001

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT ($) 27 =

Complete if Known	
Application Number	09/427,447
Filing Date	27 Oct 1999
First Named Inventor	SZYNALSKI
Examiner Name	Samuel RIMMEL
Group Art Unit	2166
Attorney Docket No.	NutriMerica

METHOD OF PAYMENT

1. ☐ The Commissioner is hereby authorized to charge indicated fees and credit any overpayments to:
   - Deposit Account Number
   - Deposit Account Name
   - ☐ Charge Any Additional Fee Required Under 37 CFR 1.16 and 1.17
   - ☐ Applicant claims small entity status. See 37 CFR 1.27

2. ☑ **Payment Enclosed:** ☐ Check ☑ Credit card ☐ Money Order ☐ Other

FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	710	201	355	Utility filing fee	
106	320	206	160	Design filing fee	
107	490	207	245	Plant filing fee	
108	710	208	355	Reissue filing fee	
114	150	214	75	Provisional filing fee	

SUBTOTAL (1) ($)

2. EXTRA CLAIM FEES

		Extra Claims		Fee from below	Fee Paid
Total Claims		-20** =	4	X 9 =	27
Independent Claims		- 3** =		X =	
Multiple Dependent				=	

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	80	202	40	Independent claims in excess of 3
104	270	204	135	Multiple dependent claim, if not paid
109	80	209	40	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL (2) ($) 27 =

**or number previously paid, if greater; For Reissues, see above

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge - late filing fee or oath	
127	50	227	25	Surcharge - late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,520	147	2,520	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	390	216	195	Extension for reply within second month	
117	890	217	445	Extension for reply within third month	
118	1,390	218	695	Extension for reply within fourth month	
128	1,890	228	945	Extension for reply within fifth month	
119	310	219	155	Notice of Appeal	
120	310	220	155	Filing a brief in support of an appeal	
121	270	221	135	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,240	241	620	Petition to revive - unintentional	
142	1,240	242	620	Utility issue fee (or reissue)	
143	440	243	220	Design issue fee	
144	600	244	300	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	710	246	355	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	710	249	355	For each additional invention to be examined (37 CFR § 1.129(b))	
179	710	279	355	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	

Other fee (specify) _____

*Reduced by Basic Filing Fee Paid **SUBTOTAL (3)** ($)

SUBMITTED BY				Complete (if applicable)	
Name (Print/Type)	Mark POHL, Esq.	Registration No. (Attorney/Agent)	35,325	Telephone	(973) 665-0275
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IN THE UNITED STATES PATENT OFFICE

Inventor : Alexander Goen SZYNALSKI
Serial No. : 09/427,447
Filing Date : 27 Oct 1999
Title : Stop Smoking Methods
Group Art Unit : 2166
Examiner : Samuel RIMELL, Esq.

Assistant Commissioner of Patents
Washington, DC 20231

AMENDMENT

Please amend pending claims 1 and 11 to read:

1. A method for helping a tobacco smoker to stop smoking, said method comprising the steps of:

(A) providing to a tobacco smoker ~~an~~ non-conditioning, educational program to educate said tobacco smoker's conscious mind, said educational program including education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) providing to said tobacco smoker at least one hypnosis program to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) providing to said tobacco smoker ~~lobelia~~ an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco,

such that said tobacco smoker can be helped to stop smoking.

11. A product to aid a tobacco smoker in ceasing to smoke tobacco, said product comprising:

(A) means for educating said tobacco smoker's conscious mind, said educational program including non-conditioning education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) means for hypnosis to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) ~~lobelia~~ an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco.

A clean copy of claims 1 and 11 thus read:

1. A method for helping a tobacco smoker to stop smoking, said method comprising the steps of:

(A) providing to a tobacco smoker a non-conditioning, educational program to educate said tobacco smoker's conscious mind, said educational program including education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) providing to said tobacco smoker at least one hypnosis program to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) providing to said tobacco smoker an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco,

such that said tobacco smoker can be helped to stop smoking.

11. A product to aid a tobacco smoker in ceasing to smoke tobacco, said product comprising:

(A) means for educating said tobacco smoker's conscious mind, said educational program including non-conditioning education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) means for hypnosis to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco.

Please withdraw the previous cancellation of claims 7, 8, 17 and 18. Please add new claims 21-24:

21. The method of claim 1, wherein said anti-smoking drug is an antidepressant.

22. The method of claim 21, wherein said antidepressant is lobelia.

23. The product of claim 11, wherein said anti-smoking drug is an antidepressant.

24. The product of claim 23, wherein said antidepressant is lobelia.

REMARKS

Claims 1, 6, 11 and 16 are pending in the application. Claims 1 and 11 stand rejected in light of Cooper *et al.*

Claims 1 and 11

Amendments are made to elements (A) and (C).

Element (A) - "an educational program"

Cooper cannot anticipate claims 1 and 11 because Cooper fails to teach an essential claim element.

The claims require three elements: "(A) education...; (B) hypnosis, to use *the unconscious mind* to stop smoking; and (C) nutritional supplements addressing the nutritional challenges with regard to stopping smoking." Specification at 1. These three elements act on "the *conscious* mind, the *unconscious* mind, and the *body*." Id.

The unconscious mind is programmed using repetition of stimuli, to take the subject toward pleasure and away from pain. Id. at 7. The Specification discusses numerous methods for programming the unconscious, id. at 7-10. Methods of programming the unconscious mind are referred to as "hypnosis." In the preferred embodiment, such hypnosis involves, for example, negative conditioning. Id. at 8. ("hypnosis focuses on interrupting 'conditioned responses' generally, and specifically, on interrupting the response to smoke").

Conditioning is "A process of behavior modification by which a subject comes to associate a desired behavior with a previously **unrelated** stimulus." American Heritage Dictionary (2000) (available at *www.dictionary.com*). Conditioning was discovered by I.P. PAVLOV, who trained dogs to perform an unconscious response (salivation) in response to an unrelated stimulus (a bell). On-Line Medical Dictionary (12 Dec 1998).

Cooper teaches a "negative conditioning" apparatus. Conditioning is a method of programming *unconscious* response. It is not an educational program for the conscious mind. The claims have been amended to clarify that "conditioning" is a type of hypnosis, not a type of education.

Element (C) - "lobelia"

Element C is broadened to encompass equivalents of lobelia literally.

The Specification teaches that lobelia is an antidepressant acetylcholine receptor binder. Specification at 13-15. The Specification teaches other examples of antidepressants, id. at 18 (gotu kola extract; kava kava root).

It is known in the art that antidepressants can be used as stop-smoking drugs. For example, buproprion hydrochloride is sold as both an antidepressant (commercially available under the trademark WELLBUTRIN® from Glaxo-Wellcome Inc., Chapel Hill, North Carolina) and a stop-smoking drug (commercially available under the trademark ZYBAN® from Glaxo-Wellcome Inc., Chapel Hill, North Carolina). Physicians' Desk Reference at 1277 *et seq.* (1999). Antidepressants "produce[] a calming effect within the body, thereby relieving the stress associated with nicotine withdrawal symptoms." Specification at 18, lines 8-9. This probably explains why individuals quitting smoking feel better when taking an anti-smoking drug. Id. at 15, lines 12-14.

Accordingly, element (C) is broadened to encompass stop-smoking drugs generally, and dependent claims 21-24 are added to recite lobelia specifically.

Claims 7, 8, 17 and 18

These claims were previously rejected as allegedly non-enabled under Section 112, first paragraph. The claims were then withdrawn based on the understanding that the remaining claims would proceed to prompt allowance. The 24 Oct 2001 Office Action moots the reason to have withdrawn these claims.

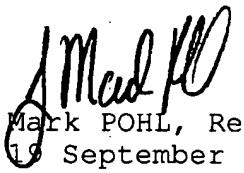
These claims comply with 35 USC 112. Claims 7 and 17 recite "at least one weight-control product." Claims 8 and 18 require the weight control product to include a stimulant.

Weight control products ("anorexants"), the use of CNS stimulants as such, and the therapeutically effective amounts, are known nearly universally in the United States. *See e.g.*, The Merck Manual at 2492-93 (1987) ("CNS stimulants are used to … suppress the appetite. *** The failure of most obese patients to lose weight satisfactorily by attempting to decrease food intake alone has led to widespread use of anorexants. Amphetamine and related compounds … are most effective for the first 3 to 6 wk."). CNS stimulants which are used as anorexants in include amphetaminil, benzphetamide, chlorphentermine, clortermine, dextroamphetamine sulfate, diethylpropion, n-ethylamphetamine, mazindol, methamphetamine, and others. *See* The Merck Index (1996). The Specification need not disclose subject matter already common knowledge in the art.

SUMMARY

All pending claims are believed patentable over the art. Prompt allowance is respectfully requested.

Respectfully Submitted,



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19 September 2001

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100 mg have been used in severely resistant patients. For maintenance, dosage is reduced to the smallest effective amount. Haloperidol is readily absorbed orally. Peak plasma concentration occurs 2 to 6 h after ingestion and may plateau for as long as 72 h; plasma levels may be detectable for weeks. In acute cases, haloperidol 2 to 5 mg IM may be given.

Haloperidol potentiates the effect of CNS depressants and anticoagulants. It diminishes the effect of L-dopa. It can diminish dyskinesia but aggravates parkinsonism in patients on L-dopa therapy. Since prolonged neuroleptic therapy is associated with development of tardive dyskinesias, haloperidol is not recommended for the treatment of tardive dyskinesias or L-dopa dyskinesias because it can mask the worsening of neuroleptic-related tardive dyskinesias.

THIOXANTHENES

Of the 4 thioxanthenes marketed in various countries, only **chlorprothixene** and **thiothixene** are available in the USA for clinical use. The thioxanthenes resemble the phenothiazines in chemical structure, absorption, metabolism, excretion, and clinical effects. Chlorprothixene and thiothixene have been used in the treatment of schizophrenia and depression. The average oral daily adult dosage is 75 to 200 mg for chlorprothixene and 10 to 30 mg for thiothixene; however, individual patient requirements vary.

Like other neuroleptics, the thioxanthenes interfere with conditioned reflex activity without affecting unconditioned reflex activity. They increase limbic system activity and inhibit proprioceptive arousal reactions. Psychoactive thioxanthenes share some of the properties of tricyclic antidepressants. Thiothixene is comparable to chlorpromazine in therapeutic impact and is particularly effective against affective symptoms. It is especially useful for patients who are socially withdrawn, and is also effective in the management of psychotic depression, tension-agitation, and anxiety.

Fever, fatigue, and drowsiness are the most frequent adverse effects. The sensitivity to sunlight seen with phenothiazines is usually not observed. The relative frequency of adverse effects with thiothixene is lower than with the corresponding phenothiazine analogs. The lower incidence of extrapyramidal effects in long-term maintenance therapy is especially advantageous. Thiothixene has fewer adverse effects on the myocardium than does thioridazine.

OTHER ANTIPSYCHOTIC DRUGS

Loxapine, a tricyclic dibenzoxazepine derivative, is chemically distinct from thioxanthenes, butyrophenones, and phenothiazines. Its pharmacologic and toxicologic properties are similar to those of the piperazine group of phenothiazines. Therapeutic efficacy is comparable with that of other neuroleptics in schizophrenia. Side effects include involuntary movements, hypotension, and somnolence. Oral doses range from 60 to 100 mg/day, although some patients may require up to 250 mg/day.

Molindone, a dihydroindolone derivative, is structurally different from the phenothiazines, butyrophenones, and thioxanthenes, but is also pharmacologically similar to the phenothiazines. The daily oral dose range is 20 to 200 mg.

GENERAL CENTRAL NERVOUS SYSTEM STIMULANTS AND ANOREXIANTS

CNS stimulants are used to increase alertness, inhibit fatigue, suppress the appetite, manage certain children with minimal brain dysfunction or hyperkinesis, and treat narcolepsy. Many of these drugs are related to amphetamine and share the phenethylamine structure. Their activity as psychostimulants is primarily due to an ability to act

indirectly by displacing endogenous catecholamines from storage sites in neural tissues, but may also be partly related to direct catecholamine-like adrenergic receptor activation in the CNS. Their use in clinical medicine continues to decline because of criticism of any use to induce brief mood elevation or to suppress fatigue and a fear that nonchalant prescribing may have contributed to abuse (see also Ch. 138).

The failure of most obese patients to lose weight satisfactorily by attempting to decrease food intake alone has led to widespread use of anorexiants. Though these drugs may be of value in beginning a weight reduction program, their long-term utility has been questioned. Amphetamine and related compounds such as diethylpropion, phentermine, and phendimetrazine are most effective for the first 3 to 6 wk. The suggestion that they might be useful intermittently over a long period to aid in weight control has been made. The dosage usually is divided and given before meals, but some agents have a long duration of action and may be given less frequently. Most anorexiants may disturb sleep if given late in the day. The use of agents less subject to abuse than amphetamine or phenmetrazine is recommended whenever feasible.

Amphetamine is the prototype CNS stimulant. There are a variety of amphetamine salts and mixtures in various formulations. Amphetamine produces mood elevation with increased wakefulness, alertness, concentration, and physical performance. Systolic and diastolic blood pressures are raised, the respiratory center is stimulated, and appetite is suppressed through a central effect. It is rapidly absorbed from the GI tract, reaches high concentrations in the CNS, and is largely metabolized. Its prolonged duration of sympathomimetic action relates to its resistance to metabolic degradation by enzymes that metabolize catecholamines. Amphetamine and related compounds, when taken repeatedly, induce tolerance to some degree, but this is partially dependent on dosage.

Insomnia, dizziness, excessive sweating, tremors, and euphoria may occur, and feelings of depression and fatigue often accompany withdrawal. Anxiety and panic states are seen, particularly at the high dosage levels associated with amphetamine abuse. Lethal overdose is uncommon because of the large difference between an effective and fatal dose and because tolerance has often occurred. For a detailed discussion of amphetamine abuse and its management, see Ch. 138.

Methylphenidate is a CNS stimulant with effects similar to that of amphetamine. It is used to treat hyperkinesis in children (see LEARNING DISORDERS in Ch. 188) and for narcolepsy (see Ch. 122).

Fenfluramine, a newer anorexiant, appears to have minimal abuse potential. Although a phenethylamine, it has sedation as its principal side effect and may be given late in the day without disturbing sleep. It should be *avoided* in patients with a history of mental depression and migraine. Some feel that a low night-time dose of fenfluramine may be combined with a daytime dose of phentermine or diethylpropion for effective and minimally symptom-inducing anorexia.

ANTIEMETICS

Drugs that prevent or relieve nausea and vomiting. Nausea and vomiting may be symptoms of disease processes, eg, metabolic or microbial toxins, or responses to stimuli such as drugs, radiation, or motion. The underlying cause should be sought and corrected if possible, as the etiology suggests which antiemetic is optimal for symptomatic treatment. Nausea and vomiting induced by noncytotoxic drugs such as digitalis, estrogens, and iron preparations should be treated by reducing the dose, changing the route of administration, or switching to another drug.

Stimulation of the vomiting center in the medulla can arise in the chemoreceptor trigger zone (**CTZ**), cerebral cortex, or vestibular apparatus, or can be relayed directly from peripheral areas (eg, gastric mucosa). Though the mechanism of action of the

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ANESTHETIC (LOCAL)

Ambucaine, *402*
Amolanone, *610*
Amylocaine Hydrochloride, *656*
Benoxinate, *1076*
Benzocaine, *1116*
Betoxycaine, *1235*
Biphenamine, *1275*
Bupivacaine, *1520*
Butacaine, *1531*
Butamben, *1538*
Butanilicaine, *1542*
Butethamine, *1552*
Butoxycaine, *1566*
Carticaine, *1920*
Chloroprocaine Hydrochloride, *2210*
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Cocaine, *2517*
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Dibucaine Hydrochloride, *3081*
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Diperodon Hydrochloride, *3360*
Dyclonine, *3523*
Ecgonidine, *3540*
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Ethyl Chloride, *3829*
Etidocaine, *3907*
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Euprocin, *3950*
Fenalcomine, *3996*
Fomocaine, *4259*
Hexylcaine Hydrochloride, *4746*
Hydroxytetracaine, *4894*
Isobutyl *p*-Aminobenzoate, *5148*
Leucinocaine Mesylate, *5476*
Levoxadrol *see 3352*
Lidocaine, *5505*
Mepivacaine, *5905*
Meprylcaine, *5909*
Metabutoxycaine, *5978*
Methyl Chloride, *6121*
Myrtecaine, *6422*
Naepaine, *6435*
Octacaine, *6839*
Orthocaine, *7011*
Oxethazaine, *7067*
Parethoxycaine, *7171*
Phenacaine Hydrochloride, *7342*
Phenol, *7390*
Piperocaine, *7627*
Piridocaine, *7649*
Polidocanol, *7717*
Pramoxine, *7888*
Prilocaine, *7924*
Procaine, *7937*
Propanocaine, *7988*
Proparacaine, *7991*
Propipocaine, *8016*
Propoxycaine Hydrochloride, *8023*
Pseudococaine, *8097*
Pyrrocaine, *8197*
Ropivacaine, *8417*
Salicyl Alcohol, *8477*
Tetracaine Hydrochloride, *9330*
Tolycaine, *9679*
Trimecaine, *9830*
Zolamine, *10319*

ANGIOTENSIN CONVERTING ENZYME INHIBITOR *see ACE-Inhibitor*

ANGIOTENSIN II RECEPTOR ANTAGONIST *see also Antihypertensive*

Candesartan, *1788*
Eprosartan, *3669*
Irbesartan, *5097*
Losartan, *5613*
Valsartan, *10051*

ANOREXIC

Aminorex, *497*
Amphecloral, *620*
Amphetamine, *623*
Benzphetamine, *1151*
Chlorphentermine, *2235*
Clobenzorex, *2421*
Cloforex, *2440*
Clortermine, *2472*
Cyclexedrine, *2776*
Dextroamphetamine Sulfate, *2996*
Diethylpropion, *3175*
Diphemethoxidine, *3362*
N-Ethylamphetamine, *3809*
Fenbutrazate, *4005*
Fenfluramine, *4015*
Fenproporex, *4036*
Furfurylmethylamphetamine, *4327*
Levophacetoperane, *5493*
Mazindol, *5801*
Mefenorex, *5843*
Metamfepramone, *5984*
Methamphetamine, *6015*
Norpseudoephedrine, *6811*
Pentorex, *7275*
Phendimetrazine, *7365*
Phenmetrazine, *7385*
Phentermine, *7415*
Phenylpropanolamine Hydrochloride, *7461*
Picilorex, *7551*
Sibutramine, *8629*

ANTACID

Alexitol Sodium, *232*
Almagate, *307*
Aluminum Hydroxide, *355*
Aluminum Magnesium Silicate, *362*
Aluininum Phosphate, *371*
Azulene, *956*
Basic Aluminum Carbonate Gel, *1033*
Bismuth Aluminate, *1298*
Bismuth Phosphate, *1316*
Bismuth Subgallate, *1325*
Bismuth Subnitrate, *1326*
Calcium Carbonate, *1697*
Dihydroxyaluminum Aminoacetate, *3227*
Dihydroxyaluminum Sodium Carbonate, *3228*
Ebirnar, *3535*
Magaldrate, *5685*
Magnesium Carbonate Hydroxide, *5696*
Magnesium Hydroxide, *5706*
Magnesium Oxide, *5713*
Magnesium Peroxide, *5717*
Magnesium Phosphate, Tribasic, *5720*
Magnesium Silicates, *5727*
Potassium Citrate, *7785*
Sodium Bicarbonate, *8726*

ANTHELMINTIC (CESTODES)

Arecoline, *815*
Aspidin, *881*
Aspidinol, *882*
Dichlorophen(e), *3120*
Embelin, *3595*
Kosin, *5333*

...ers
...Bencyclane, *1060*
...Bufenone, *3753*
...Pantofarone, *3975*
...Perhexiline, *7305*

...IUM REGULATOR
...Calcifediol, *1677*
...Calcitonin, *1680*
...Calcitriol, *1681*
...Dihydrotachysterol, *3223*
...Elcatonin, *3578*
...Isoflavone, *5090*
...Parathyroid Hormone, *7168*
...Teriparatide Acetate, *9309*

...UM SUPPLEMENT *see Replen-...Supplements*

...ER CHEMOTHERAPY *see ...toplastic*

...LARY PROTECTANT *see ...protectant*

...ONIC ANHYDRASE INHIBI-... *see also Antiglaucoma; Diuretic*
...Acetazolamide, *50*
...Butazolamide, *1545*
...Dichlorphenamide, *3127*
...Dorzolamide, *3484*
...Ethoxzolamide, *3801*
...Hydrochlorothiazide, *4174*
...Methazolamide, *6031*

...AC DEPRESSANT (ANTIAR-...THMIC) *see Antiarrhythmic*

...OTONIC
...Acetylline, *22*
...Acetyldigitoxins, *90*
...Amino-4-picoline, *486*
...Amrinone, *634*
...Benfurodil Hemisuccinate, *1070*
...Butladesine, *1782*
...Camphotamide, *1782*
...Convallatoxin, *2575*
...Cymarin, *2830*
...Dehopamine, *2943*
...Deslanoside, *2967*
...Digitalin, *3200*
...Digitalis, *3201*
...Digitoxin, *3206*
...Digoxin, *3210*
...Dobutamine, *3456*
...Dopacarpamine, *3457*
...Dopamine, *3479*
...Dopexamine, *3482*
...Enoximone, *3627*
...Erythrophleine, *3728*
...Fendilcomine, *3996*
...Gitalin, *4437*
...Gitoxin, *4441*
...Hydrocyamine, *4505*
...Ibopamine, *4691*
...Lanatinine, *4807*
...Levamine, *4921*
...Lanatosides, *5368*
...Milrinone, *5605*
...Olprinone, *6284*
...Pentifolin, *6559*
...Quadrin, *6963*
Ouabain, *7031*
Oxyfedrine, *7096*
Pimobendan, *7588*
Prenalterol, *7917*
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Resibufogenin, *8315*
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Scillarenin, *8544*
Strophanthin, *9016*
Sulmazole, *9159*
Theobromine, *9418*
Vesnarinone, *10105*
Xamoterol, *10189*

CATHARTIC *see Laxative/Cathartic*

CATION-EXCHANGE RESIN *see Ion-exchange Resin*

CCK ANTAGONIST
Loxiglumide, *5618*
Proglumide, *7958*

CENTRAL STIMULANT *see CNS Stimulant*

CEREBRAL VASODILATOR *see Vasodilator (Cerebral)*

CHELATING AGENT
Deferoxamine, *2914*
Ditiocarb Sodium, *3443*
Edetate Calcium Disodium, *3555*
Edetate Disodium, *3556*
Edetate Sodium, *3557*
Edetate Trisodium, *3558*
Penicillamine, *7214*
Pentetate Calcium Trisodium, *7265*
Pentetic Acid, *7266*
Succimer, *9034*
Trientine, *9796*

CHOLECYSTOKININ ANTAGONIST *see CCK Antagonist*

CHOLELITHOLYTIC AGENT
Chenodiol, *2096*
Methyl *tert*-Butyl Ether, *6111*
Monoctanoin, *6335*
Ursodiol, *10026*

CHOLERETIC
Alibendol, *243*
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Azintamide, *945*
Cholic Acid, *2258*
Cicrotoic Acid, *2327*
Clanobutin, *2398*
Cyclobutyrol, *2784*
Cyclovalone, *2823*
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Dehydrocholic Acid, *2922*
Deoxycholic Acid, *2946*
Dimecrotic Acid, *3248*
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Exiproben, *3959*
Febuprol, *3985*
Fencibutirol, *4009*
Fenipentol, *4016*
Florantyrone, *4143*
Hymecromone, *4903*
Menbutone, *5878*
3-(o-Methoxyphenyl)-2-phenylacrylic Acid, *5880*
Metochalcone, *6225*
Moquizone, *6347*
Osalmid, *7018*
Ox Bile Extract, *7052*
4,4'-Oxydi-2-butanol, *7094*
Piprozolin, *7639*
4-Salicyloylmorpholine, *8485*
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Tocamphyl, *9630*
Trepibutone, *9718*
Vanitiolide, *10071*

CHOLINERGIC
Aceclidine *see 8266*
Acetylcholine Bromide, *87*
Acetylcholine Chloride, *88*
Aclatonium Napadisilate, *116*
Benzpyrinium Bromide, *1153*
Bethanechol Chloride, *1232*
Carbachol, *1823*
Carpronium Chloride, *1913*
Demecarium Bromide, *2936*
Dexpanthenol, *2988*
Diisopropyl Paraoxon, *3242*
Echothiophate Iodide, *3549*
Edrophonium Chloride, *3562*
Eptastigmine, *3672*
Eseridine, *3740*
Furtrethonium, *4334*
Isoflurophate, *5192*
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Muscarine, *6389*
Neostigmine, *6553*
Oxapropanium Iodide, *7056*
Physostigmine, *7540*
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Xanomeline, *10190*

CHOLINESTERASE INHIBITOR
Ambenonium Chloride, *396*
Distigmine Bromide, *3426*
Eptastigmine, *3672*
Galanthamine, *4357*

CHOLINESTERASE REACTIVATOR
Asoxime Chloride, *870*
Obidoxime Chloride, *6835*
Pralidoxime Chloride, *7884*

CNS STIMULANT
Amineptine, *429*
Amphetamine, *623*
— Amphetaminil, *624*
Bemegride, *1054*
— Benzphetamine, *1151*
Brucine, *1476*
Caffeine, *1674*
— Chlorphentermine, *2235*
— Clortermine, *2472*
Coca, *2515*
Deanol, *2900*
Demanyl Phosphate, *2935*
Dexoxadrol *see 3352*
— Dextroamphetamine Sulfate, *2996*
— Diethylpropion, *3175*
— *N*-Ethylamphetamine, *3809*
Ethamivan, *3765*
Etifelmin, *3919*
Etryptamine, *3937*
Fencamfamine, *4006*

CNS STIMULANT (*continued*)

Fenethylline, *4014*
Fenozolone, *4028*
Flurothyl, *4236*
Hexacyclonate Sodium, *4717*
Homocamfin, *4768*
Mazindol, *5801*
Mefexamide, *5844*
Methamphetamine, *6015*
Methylphenidate, *6186*
Modafinil, *6311*
Nikethamide, *6635*
Pemoline, *7206*
Pentylenetetrazole, *7283*
Phendimetrazine, *7365*
Phenmetrazine, *7385*
Phentermine, *7415*
Picrotoxin, *7570*
Pipradrol, *7638*
Prolintane, *7964*
Pyrovalerone, *8194*

COGNITION ACTIVATOR *see Nootropic*

CONTRACEPTIVE (INJECTABLE)

Medroxyprogesterone, *5838*
Norethindrone, *6790*

CONTRACEPTIVE (ORAL)

Desogestrel, *2971*
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Ethynodiol, *3905*
Gestodene, *4421*
Lynestrenol, *5659*
Mestranol, *5976*
Norethindrone, *6790*
Norethynodrel, *6791*
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Norgestrel, *6797*

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Apraclonidine, *791*

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CORONARY VASODILATOR *see Vasodilator (Coronary)*

CYTOPROTECTANT (GASTRIC) *see also Antiulcerative*

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Guaiazulene, *4581*
Irsogladine, *5113*
Plaunotol, *7692*
Polaprezinc, *7712*
Rebamipide, *8296*
Sofalcone, *8850*
Spizofurone, *8918*
Sucralfate, *9049*
Teprenone, *9296*
Troxipide, *9921*
Zolimidine, *10320*

DEBRIDING AGENT

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Papain, *7148*

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Epinephrine, *3656*
Fenoxazoline, *4025*
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Oxymetazoline, *7100*
Phenylephrine Hydrochloride, *7440*
Phenylpropanolamine Hydrochloride, *7461*
Phenylpropylmethylamine, *7462*
Propylhexedrine, *8045*
Pseudoephedrine *see 3641*
Tetrahydrozoline, *9358*
Tramazoline, *9702*
Tuaminoheptane, *9934*
Tymazoline, *9965*
Xylometazoline, *10219*

DEPIGMENTOR

Hydroquinine, *4852*
Hydroquinone, *4853*
Monobenzone, *6331*

DERMATITIS HERPETIFORMIS SUPPRESSANT

Dapsone, *2885*
Sulfapyridine, *9108*

DIAGNOSTIC AID

Alsactide, *322*
Americium, *410*
p-Aminohippuric Acid, *462*
Anazolene Sodium, *669*
Arbutamine, *811*
Arginine, *817*
Bentiromide, *1081*
Betazole, *1230*
Ceruletide, *2048*
Colfosceril Palmitate, *2540*
Congo Red, *2562*
Dexamethasone, *2986*
Edrophonium Chloride, *3562*
Evan's Blue, *3952*
Fluorescein, *4194*
Galactose, *4353*
Glycerol, *4493*
Histamine, *4756*
Indocyanine Green, *4992*
Inulin, *5024*
Iodinated Serum Albumin *see 8613*
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Mannitol, *5788*
Merisoprol Hg 197, *5959*
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Metyrapone, *6246*
Oleic Acid, *6965*
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Pentagastrin, *7250*
Phenolsulfonphthalein, *7397*
Phenoltetrachlorophthalein, *7398*
Phentolamine, *7417*
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Rose Bengal, *8421*
Saralasin, *8518*
Sodium Benzoate, *8725*
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Sodium Iodide, Radioactive
Sulfobromophthalein Sodium
Teriparatide Acetate, *9307*
Tolonium Chloride, *9651*
TSH, *9931*
Tuberculin, *9937*
Tubocurarine Chloride
Vitamin B_{12}, Radioactive
Xylose, *10220*

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Perflubron, *7299*

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Disofenin Complex with ^{99m}Tc *see 3422*
Exametazime Complex with ^{99m}Tc *see 3957*
Fludeoxyglucose F^{18}, *4163*
Iobenguane, *5027*
Iofetamine ^{123}I, *5066*
Lidofenin Complex with *5506*
Medronic Acid Complex with ^{99m}Tc *see 5837*
Oxidronic Acid Complex with ^{99m}Tc *see 7074*
Panidronic Acid Complex with ^{99m}Tc *see 7135*
Pentetreotide Chelate with *7267*
Satumomab Pendetide *8530*
Sodium Pertechnetate
Sodium Phosphate, Radioactive *8807*
Stannous Pyrophosphate with ^{99m}Tc *see 8945*
Succimer Complex with *9034*
Technetium, *9256*
Technetium ^{99m}Tc Bicisate
Technetium ^{99m}Tc Mertiatide
Technetium ^{99m}Tc Sestamibi
Technetium ^{99m}Tc Tetrofosmin *9260*
Tetrofosmin Complex with *see 9383*
^{133}Xenon *see 10206*

DIAGNOSTIC AID (RADIOPAQUE MEDIUM)

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Barium Sulfate, *1023*
Bunamiodyl Sodium
Diatrizoate Sodium
Ethiodized Oil, *3781*
Iobenzamic Acid, *5028*
Iocarmic Acid, *5029*
Iocetamic Acid, *5030*
Iodipamide, *5043*
Iodixanol, *5044*

PDR®

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DOSAGE AND ADMINISTRATION

CAUTION— RAPID OR BOLUS INTRAVENOUS AND INTRAMUSCULAR OR SUBCUTANEOUS INJECTION MUST BE AVOIDED. Therapy should be initiated as early as possible following onset of signs and symptoms. For diagnosis—see INDICATIONS.

Dosage: ***Herpes Simplex Infections: Mucosal and Cutaneous Herpes Simplex (HSV-1 and HSV-2) Infections in Immunocompromised Patients:*** 5 mg/kg infused at a constant rate over 1 hour, every 8 hours (15 mg/kg/day) for 7 days in adult patients with normal renal function. In pediatric patients under 12 years of age, more accurate dosing can be attained by infusing 250 mg/m^2 at a constant rate over 1 hour, every 8 hours (750 mg/m^2/day) for 7 days.

Severe Initial Clinical Episodes of Herpes Genitalis: The same dose given above—administered for 5 days.

Herpes Simplex Encephalitis: 10 mg/kg infused at a constant rate over at least 1 hour, every 8 hours for 10 days. In pediatric patients between 6 months and 12 years of age, more accurate dosing is achieved by infusing 500 mg/m^2, at a constant rate over at least 1 hour, every 8 hours for 10 days.

Varicella Zoster Infections: Zoster in Immunocompromised Patients: 10 mg/kg infused at a constant rate over 1 hour, every 8 hours for 7 days in adult patients with normal renal function. In pediatric patients under 12 years of age, equivalent plasma concentrations are attained by infusing 500 mg/m^2 at a constant rate over at least 1 hour, every 8 hours for 7 days. Obese patients should be dosed at 10 mg/kg (Ideal Body Weight). A maximum dose equivalent to 500 mg/m^2 every 8 hours should not be exceeded for any patient.

Patients with Acute or Chronic Renal Impairment: Refer to DOSAGE AND ADMINISTRATION section for recommended doses, and adjust the dosing interval as indicated in the table below.

Creatinine Clearance (mL/min/1.73 m^2)	Percent of Recommended Dose	Dosing Interval (hours)
>50	100%	8
25–50	100%	12
10–25	100%	24
0–10	50%	24

Hemodialysis: For patients who require dialysis, the mean plasma half-life of acyclovir during hemodialysis is approximately 5 hours. This results in a 60% decrease in plasma concentrations following a 6-hour dialysis period. Therefore, the patient's dosing schedule should be adjusted so that an additional dose is administered after each dialysis.[24,25]

Peritoneal Dialysis: No supplemental dose appears to be necessary after adjustment of the dosing interval.[40, 41]

Method of Preparation: Each 10-mL vial contains acyclovir sodium equivalent to 500 mg of acyclovir. Each 20-mL vial contains acyclovir sodium equivalent to 1000 mg of acyclovir. The contents of the vial should be dissolved in Sterile Water for Injection as follows:

Contents of Vial	Amount of Diluent
500 mg	10 mL
1000 mg	20 mL

The resulting solution in each case contains 50 mg acyclovir per mL (pH approximately 11). Shake the vial well to assure complete dissolution before measuring and transferring each individual dose. DO NOT USE BACTERIOSTATIC WATER FOR INJECTION CONTAINING BENZYL ALCOHOL OR PARABENS.

Administration: The calculated dose should then be removed and added to any appropriate intravenous solution at a volume selected for administration during each 1-hour infusion. Infusion concentrations of approximately 7 mg/mL or lower are recommended. In clinical studies, the average 70-kg adult received between 60 and 150 mL of fluid per dose. Higher concentrations (e.g., 10 mg/mL) may produce phlebitis or inflammation at the injection site upon inadvertent extravasation. Standard, commercially available electrolyte and glucose solutions are suitable for intravenous administration; biologic or colloidal fluids (e.g., blood products, protein solutions, etc.) are not recommended.

Once in solution in the vial at a concentration of 50 mg/mL, the drug should be used within 12 hours. Once diluted for administration, each dose should be used within 24 hours. Refrigeration of reconstituted solutions may result in formation of a precipitate which will redissolve at room temperature.

HOW SUPPLIED

...containing acyclovir sodium equivalent to 500 mg of acyclovir, tray of 10 (NDC 0173-0952-00).

20-mL sterile vials, each containing acyclovir sodium equivalent to 1000 mg of acyclovir, tray of 10 (NDC 0173-0952-01).

Store at 15° to 25°C (59° to 77°F).

REFERENCES

1. O'Brien JJ, Campoli-Richards DM. Acyclovir—an updated review of its antiviral activity, pharmacokinetic properties and therapeutic efficacy. *Drugs.* 1989;37:233-309.
2. Littler E, Zeuthen J, McBride AA, et al. Identification of an Epstein-Barr virus-coded thymidine kinase. *EMBO J.* 1986;5:1959-1966.
3. Miller WH, Miller RL. Phosphorylation of acyclovir (acycloguanosine) monophosphate by GMP kinase. *J Biol Chem.* 1980;255:7204-7207.
4. Furman PA, St Clair MH, Fyfe JA, et al. Inhibition of herpes simplex virus-induced DNA polymerase activity and viral DNA replication by 9-(2-hydroxyethoxymethyl)guanine and its triphosphate. *J Virol.* 1979;32:72-77.
5. Derse D, Cheng YC, Furman PA, et al. Inhibition of purified human and herpes simplex virus-induced DNA polymerases by 9-(2-hydroxyethoxymethyl)guanine triphosphate: effects on primer-template function. *J Biol Chem.* 1981;256:11447-11451.
6. McGuirt PV, Shaw JE, Elion GB, et al. Identification of small DNA fragments synthesized in herpes simplex virus-infected cells in the presence of acyclovir. *Antimicrob Agents Chemother.* 1984;25:507-509.
7. Barry DW, Blum MR. Antiviral drugs: acyclovir. In: Turner P, Shand DG, eds. *Recent Advances in Clinical Pharmacology.* ed 3. New York: Churchill Livingstone, 1983: chap 4.
8. DeClercq E. Comparative efficacy of antiherpes drugs in different cell lines. *Antimicrob Agents Chemother.* 1982;21:661-663.
9. McLaren C, Ellis MN, Hunter GA. A colorimetric assay for the measurement of the sensitivity of herpes simplex viruses to antiviral agents. *Antiviral Res.* 1983;3:223-234.
10. Barry DW, Nusinoff-Lehrman S. Viral resistance in clinical practice: summary of five years experience with acyclovir. In: Kono R, Nakajima A, eds. *Herpes Viruses and Virus Chemotherapy (Ex Med Int Congr Ser 667).* New York: *Excerpta Medica,* 1985;269-270.
11. Dekker C, Ellis MN, McLaren C, et al. Virus resistance in clinical practice. *J Antimicrob Chemother.* 1983;12 (suppl B):137-152.
12. Sibrack CD, Gutman LT, Wilfert CM, et al. Pathogenicity of acyclovir-resistant herpes simplex virus type 1 from an immunodeficient child. *J Infect Dis.* 1982;146: 673-682.
13. Crumpacker CS, Schnipper LE, Marlowe SI, et al. Resistance to antiviral drugs of herpes simplex virus isolated from a patient treated with acyclovir. *N Engl J Med.* 1982;306:343-346.
14. Wade JC, Newton B, McLaren C, et al. Intravenous acyclovir to treat mucocutaneous herpes simplex virus infection after marrow transplantation: a double-blind trial. *Ann Intern Med.* 1982;96:265-269.
15. Burns WH, Saral R, Santos GW, et al. Isolation and characterization of resistant herpes simplex virus after acyclovir therapy. *Lancet.* 1982;1:421-423.
16. Straus SE, Takiff HE, Seidlin M, et al. Suppression of frequently recurring genital herpes: a placebo-controlled double-blind trial of oral acyclovir. *N Engl J Med.* 1984;310:1545-1550.
17. Collins P. Viral sensitivity following the introduction of acyclovir. *Am J Med.* 1988;85(suppl 2A):129-134.
18. Erlich KS, Mills J, Chatis P, et al. Acyclovir-resistant herpes simplex virus infections in patients with the acquired immunodeficiency syndrome. *N Engl J Med.* 1989;320:293-296.
19. Hill EL, Ellis MN, Barry DW. In: *28th Intersci Conf on Antimicrob Agents Chemother.* Los Angeles, 1988, Abst. No. 0840:260.
20. Ellis MN, Keller PM, Fyfe JA, et al. Clinical isolates of herpes simplex virus type 2 that induces a thymidine kinase with altered substrate specificity. *Antimicrob Agents Chemother.* 1987;31:1117-1125.
21. Collins P, Larder BA, Oliver NM, et al. Characterization of a DNA polymerase mutant of herpes simplex virus from a severely immunocompromised patient receiving acyclovir. *J Gen Virol.* 1989;70:375-382.
22. Field HJ, Darby G, Wildy P. Isolation and characterization of acyclovir-resistant mutants of herpes simplex virus. *J Gen Virol.* 1980;49:115-124.
23. Blum MR, Liao SH, deMiranda P. Overview of acyclovir pharmacokinetic disposition in adults and children. *Am J Med.* 1982;73:186-192.
24. Laskin OL, Longstreth JA, Whelton A, et al. Effect of renal failure on the pharmacokinetics of acyclovir. *Am J Med.* 1982:73:197-201.
hemodialysis on acyclovir pharmacokinetics in patients with chronic renal failure. *Am J Med.* 1982;73:202-204.
26. Mitchell CD, Bean B, Gentry SR, et al. Acyclovir therapy for mucocutaneous herpes simplex infections in immunocompromised patients. *Lancet.* 1981;1:1389-1392.
27. Meyers JD, Wade JC, Mitchell CD, et al. Multicenter collaborative trial of intravenous acyclovir for treatment of mucocutaneous herpes simplex virus infection in the immunocompromised host. *Am J Med.* 1982;73: 229-235.
28. Data on file, Glaxo Wellcome Inc.
29. Corey L, Fife KH, Benedetti JK, et al. Intravenous acyclovir for the treatment of primary genital herpes. *Ann Intern Med.* 1983;98:914-921.
30. Mindel A, Adler MW, Sutherland S, et al. Intravenous acyclovir treatment for primary genital herpes. *Lancet.* 1982;1:697-700.
31. Whitley RJ, Alford CA, Hirsch MS, et al. Vidarabine versus acyclovir therapy in herpes simplex encephalitis. *N Engl J Med.* 1986;314:144-149.
32. Sköldenberg B, Forsgren M, Alestig K, et al. Acyclovir versus vidarabine in herpes simplex encephalitis: randomized multicenter study in consecutive Swedish patients. *Lancet.* 1984;2:707-711.
33. Balfour HH Jr, Bean B, Laskin OL, et al. Acyclovir halts progression of herpes zoster in immunocompromised patients. *N Engl J Med.* 1983;308:1448-1453.
34. Shepp DH, Danliker PS, Meyers JD. Treatment of varicella-zoster virus infection in severely immunocompromised patients. *N Engl J Med.* 1986;314:208-212.
35. Naib ZM, Nahmias AJ, Josey WE, et al. Relation of cytohistopathology of genital herpesvirus infection to cervical anaplasia. *Cancer Res.* 1973;33:1452-1463.
36. Laskin OL, deMiranda P, King DH, et al. Effects of probenecid on the pharmacokinetics and elimination of acyclovir in humans. *Antimicrob Agents Chemother.* 1982;21:804-807.
37. Stahlmann R, Klug S, Lewandowski C, et al. Teratogenicity of acyclovir in rats. *Infection.* 1987;15:261-262.
38. Lau RJ, Emery MG, Galinsky RE, et al. Unexpected accumulation of acyclovir in breast milk with estimate of infant exposure. *Obstet Gynecol.* 1987;69:468-471.
39. Meyer LJ, deMiranda P, Sheth N, et al. Acyclovir in human breast milk. *Am J Obstet Gynecol.* 1988;158:586-588.
40. Boelart J, Schurgers M, Daneels R, et al. Multiple dose pharmacokinetics of intravenous acyclovir in patients on continuous ambulatory peritoneal dialysis. *J Antimicrob Chemother.* 1987;20:69-76.
41. Shah GM, Winer RL, Krasny HC. Acyclovir pharmacokinetics in a patient on continuous ambulatory peritoneal dialysis. *Am J Kidney Dis.* 1986;7:507-510.

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Shown in Product Identification Guide, page 315

ZYBAN™ B

[*zi' ban*]

(bupropion hydrochloride)

Sustained-Release Tablets

DESCRIPTION

ZYBAN (bupropion hydrochloride) Sustained-Release Tablets are a non-nicotine aid to smoking cessation. Initially developed and marketed as an antidepressant (WELLBUTRIN® [bupropion hydrochloride] Tablets and WELLBUTRIN® SR [bupropion hydrochloride] Sustained-Release Tablets), ZYBAN is chemically unrelated to tricyclic, tetracyclic, selective serotonin re-uptake inhibitor, or other known antidepressant agents. Its structure closely resembles that of diethylpropion; it is related to phenylethylamines. It is (±)-1-(3-chlorophenyl)-2-[(1,1-dimethylethyl)amino]-1-propanone hydrochloride. The molecular weight is 276.2. The molecular formula is $C_{13}H_{18}ClNO \cdot HCl$. Bupropion hydrochloride powder is white, crystalline, and highly soluble in water. It has a bitter taste and produces the sensation of local anesthesia on the oral mucosa.

ZYBAN is supplied for oral administration as 150-mg (pumple), film-coated, sustained-release tablets. Each tablet contains the labeled amount of bupropion hydrochloride and the inactive ingredients carnauba wax, cysteine hydrochloride, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, polysorbat

Continued on next page

This product information is based on labeling in effect on Jur 1, 1998. For further information, contact via direct mail, phon or web site Medical Information: Glaxo Wellcome Inc., PO Bo 13398, Research Triangle Park, NC 27709. Healthca Professionals (Medical Information): 800-334-0089 Patien (Customer Response Center): 888-TALK2GW (1-888-825-524 Glaxo Wellcome Corporate Web Site: www.glaxowellcome.co

Table 2: Comparative Trial: Quit Rates by Treatment Group

	Treatment Groups			
Abstinence From Week 4 Through Specified Week	Placebo (n = 160) % (95% CI)	Nicotine Transdermal System (NTS) 21 mg/day (n = 244) % (95% CI)	ZYBAN™ 300 mg/day (n = 244) % (95% CI)	ZYBAN 300 mg/day and NTS 21 mg/day (n = 245) % (95% CI)
Week 7 (4-week quit)	23% (17-30)	36%* (30-42)	49%*† (43-56)	58%*†‡ (51-64)
Week 10	20% (14-26)	32%* (26-37)	46%*† (39-52)	51%*† (45-58)

*. $P<0.01$ versus placebo
†. $P<0.01$ versus NTS
‡. $P=0.06$ versus ZYBAN

should not be used. **The seizure rate associated with doses of sustained-release bupropion up to 300 mg/day is approximately 0.1% (1/1,000). This incidence was prospectively determined during an 8-week treatment exposure in approximately 3,100 depressed patients. Data for the immediate-release formulation of bupropion revealed a seizure incidence of approximately 0.4% (4/1,000) in depressed patients treated at doses in a range of 300 to 450 mg/day. In addition, the estimated seizure incidence increases almost tenfold between 450 and 600 mg/day.**

- **Patient factors: Predisposing factors that may increase the risk of seizure with bupropion use include history of head trauma or prior seizure, central nervous system (CNS) tumor, and concomitant medications that lower seizure threshold.**
- **Clinical situations: Circumstances associated with an increased seizure risk include, among others, excessive use of alcohol; abrupt withdrawal from alcohol or other sedatives; addiction to opiates, cocaine, or stimulants; use of over-the-counter stimulants and anorectics; and diabetes treated with oral hypoglycemics or insulin.**
- **Concomitant medications: Many medications (e.g., antipsychotics, antidepressants, theophylline, systemic steroids) and treatment regimens (e.g., abrupt discontinuation of benzodiazepines) are known to lower seizure threshold.**

Recommendations for Reducing the Risk of Seizure: Retrospective analysis of clinical experience gained during the development of bupropion suggests that the risk of seizure may be minimized if

- **the total daily dose of ZYBAN does *not* exceed 300 mg (the maximum recommended dose for smoking cessation); and**
- **the recommended daily dose for most patients (300 mg/day) is administered in divided doses (150 mg twice daily).**
- **No single dose should exceed 150 mg to avoid high peak concentrations of bupropion and/or its metabolites.**
- **ZYBAN should be administered with extreme caution to patients with a history of seizure, cranial trauma, or other predisposition(s) toward seizure, or patients treated with other agents (e.g., antipsychotics, antidepressants, theophylline, systemic steroids, etc.) or treatment regimens (e.g., abrupt discontinuation of a benzodiazepine) that lower seizure threshold.**

Potential for Hepatotoxicity: In rats receiving large doses of bupropion chronically, there was an increase in incidence of hepatic hyperplastic nodules and hepatocellular hypertrophy. In dogs receiving large doses of bupropion chronically, various histologic changes were seen in the liver, and laboratory tests suggesting mild hepatocellular injury were noted.

PRECAUTIONS

General: ***Allergic Reactions:*** Anaphylactoid reactions characterized by symptoms such as pruritus, urticaria, angioedema, and dyspnea requiring medical treatment have been reported at a rate of about 1-3 per thousand in clinical trials of ZYBAN. In addition, there have been rare spontaneous postmarketing reports of erythema multiforme, Stevens-Johnson syndrome, and anaphylactic shock associated with bupropion.

Insomnia: In the dose-response smoking cessation trial, 29% of patients treated with 150 mg/day of ZYBAN and 35% of patients treated with 300 mg/day of ZYBAN experienced insomnia, compared to 21% of placebo-treated patients. Symptoms were sufficiently severe to require discontinuation of treatment in 0.6% of patients treated with ZYBAN and none of the patients treated with placebo.

In the comparative trial, 40% of the patients treated with 300 mg/day of ZYBAN, 28% of the patients treated with 21 mg/day of NTS, and 45% of the patients treated with the combination of ZYBAN and NTS experienced insomnia compared to 18% of placebo-treated patients. Symptoms were sufficiently severe to require discontinuation of treatment in 0.8% of patients treated with ZYBAN and none of the patients in the other three treatment groups.

Insomnia may be minimized by avoiding bedtime doses and, if necessary, reduction in dose.

Psychosis, Confusion, and Other Neuropsychiatric Phenomena: In clinical trials with ZYBAN conducted in non-depressed smokers, the incidence of neuropsychiatric side effects was generally comparable to placebo. Depressed patients treated with bupropion in depression trials have been reported to show a variety of neuropsychiatric signs and symptoms including delusions, hallucinations, psychosis, concentration disturbance, paranoia, and confusion. In some cases, these symptoms abated upon dose reduction and/or withdrawal of treatment.

Activation of Psychosis and/or Mania: Antidepressants can precipitate manic episodes in bipolar disorder patients during the depressed phase of their illness and may activate latent psychosis in other susceptible individuals. The sustained-release formulation of bupropion is expected to pose similar risks. There were no reports of activation of psychosis or mania in clinical trials with ZYBAN conducted in non-depressed smokers.

Use in Patients With Systemic Illness: There is no clinical experience establishing the safety of ZYBAN in patients with a recent history of myocardial infarction or unstable heart disease. Therefore, care should be exercised if it is used in these groups. Bupropion was well tolerated in depressed patients who had previously developed orthostatic hypotension while receiving tricyclic antidepressants, and was generally well tolerated in a group of 36 depressed inpatients with stable CHF. However, bupropion was associated with a rise in supine blood pressure in the study of patients with CHF, resulting in discontinuation of treatment in two patients for exacerbation of baseline hypertension.

In the comparative trial, 6.1% of patients treated with the combination of ZYBAN and NTS had treatment-emergent hypertension compared to 2.5%, 1.6%, and 3.1% of patients treated with ZYBAN, NTS, and placebo, respectively. The majority of these patients had evidence of preexisting hypertension. Three patients (1.2%) treated with the combination of ZYBAN and NTS and one patient (0.4%) treated with NTS had study medication discontinued due to hypertension compared to none of the patients treated with ZYBAN or placebo. Monitoring for treatment-emergent hypertension is recommended in patients receiving the combination of ZYBAN and NTS.

Because bupropion hydrochloride and its metabolites are almost completely excreted through the kidney and metabolites are likely to undergo conjugation in the liver prior to urinary excretion, treatment of patients with renal or hepatic impairment should be initiated at reduced dosage as bupropion and its metabolites may accumulate in such patients to a greater extent than usual. The patient should be closely monitored for possible toxic effects of elevated blood and tissue levels of drug and metabolites.

Information for Patients: See PATIENT INFORMATION at the end of this labeling for the text of the separate leaflet provided for patients. Physicians are advised to review the leaflet with their patients and to emphasize that ZYBAN contains the same active ingredient found in WELLBUTRIN and WELLBUTRIN SR used to treat depression and that ZYBAN should not be used in conjunction with WELLBUTRIN, WELLBUTRIN SR, or any other medications that contain bupropion hydrochloride.

Laboratory Tests: There are no specific laboratory tests recommended.

Drug Interactions: In vitro studies indicate that bupropion is primarily metabolized to hydroxybupropion by the CYP2B6 isoenzyme. Therefore, the potential exists for a drug interaction between ZYBAN and drugs that affect the CYP2B6 isoenzyme metabolism (e.g., orphenadrine and cyclophosphamide). The threohydrobupropion metabolite of bupropion does not appear to be produced by the cytochrome P450 isoenzymes. No systemic data have been collected on the metabolism of ZYBAN following concomitant administration with other drugs or, alternatively, the effect of concomitant administration of ZYBAN on the metabolism of other drugs.

Animal data indicated that bupropion may be an inducer of drug-metabolizing enzymes in humans. However, following chronic administration of bupropion, 100 mg t.i.d. to healthy male volunteers for 14 days, there was no evidence of induction of its own metabolism. Because bupropion is extensively metabolized, the coadministration of other drugs may affect its clinical activity. In particular, certain drugs may induce the metabolism of bupropion (e.g., carbamazepine, phenobarbital, phenytoin), while other drugs may inhibit the metabolism of bupropion (e.g., cimetidine).

Studies in animals demonstrate that the acute toxicity of bupropion is enhanced by the MAO inhibitor phenelzine (see CONTRAINDICATIONS).

Limited clinical data suggest a higher incidence of adverse experiences in patients receiving concurrent administration of bupropion and levodopa. Administration of ZYBAN to patients receiving levodopa concurrently should be undertaken with caution, using small initial doses and gradual dose increases.

Concurrent administration of ZYBAN and agents (e.g., antipsychotics, antidepressants, theophylline, systemic steroids, etc.) or treatment regimens (e.g., abrupt discontinuation of benzodiazepines) that lower seizure threshold should be undertaken only with extreme caution (see WARNINGS).

Physiological changes resulting from smoking cessation itself, with or without treatment with ZYBAN, may alter the pharmacokinetics of some concomitant medications, which may require dosage adjustment.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Lifetime carcinogenicity studies were performed in rats and mice at doses up to 300 and 150 mg/kg per day, respectively. These doses are approximately ten and two times the maximum recommended human dose (MRHD), respectively, on a mg/m^2 basis. In the rat study, there was an increase in nodular proliferative lesions of the liver at doses of 100 to 300 mg/kg per day (approximately three to ten times the MRHD on a mg/m^2 basis); lower doses were not tested. The question of whether or not such lesions may be precursors of neoplasms of the liver is currently unresolved. Similar liver lesions were not seen in the mouse study, and no increase in malignant tumors of the liver and other organs was seen in either study.

Bupropion produced a positive response (two to three times control mutation rate) in two of five strains in the Ames bacterial mutagenicity test and an increase in chromosomal aberrations in one of three in vivo rat bone marrow cytogenetic studies.

A fertility study in rats at doses up to 300 mg/kg revealed no evidence of impaired fertility.

Pregnancy, Teratogenic Effects: Pregnancy Category B: Teratology studies have been performed at doses up to 450 mg/kg in rats (approximately 14 times the MRHD on a mg/m^2 basis), and at doses up to 150 mg/kg in rabbits (approximately 10 times the MRHD on a mg/m^2 basis). There is no evidence of impaired fertility or harm to the fetus due to bupropion. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed. Pregnant smokers should be encouraged to attempt cessation using educational and behavioral interventions before pharmacological approaches are used.

To monitor fetal outcomes of pregnant women exposed to ZYBAN, Glaxo Wellcome Inc. maintains a Bupropion Pregnancy Registry. Health care providers are encouraged to register patients by calling (800) 722-9292, ext. 39441.

Labor and Delivery: The effect of ZYBAN on labor and delivery in humans is unknown.

Nursing Mothers: Bupropion and its metabolites are secreted in human milk. Because of the potential for serious adverse reactions in nursing infants from ZYBAN, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use: Clinical trials with ZYBAN did not include individuals under the age of 18. Therefore, the safety and efficacy in a pediatric smoking population have not been established. The immediate-release formulation of bupropion

Continued on next page

This product information is based on labeling in effect on June 1, 1998. For further information, contact via direct mail, phone, or web site Medical Information: Glaxo Wellcome Inc., PO Box 13398, Research Triangle Park, NC 27709. Healthcare Professionals (Medical Information): 800-334-0089. Patients (Customer Response Center): 888-TALK2GW (1-888-825-5249). Glaxo Wellcome Corporate Web Site: www.glaxowellcome.com

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studied in 104 pediatric patients (age range, 6 to 16) in cal trials of the drug for other indications. Although erally well tolerated, the limited exposure is insufficient ssess the safety of bupropion in pediatric patients.

in the Elderly: In general, older patients are known to abolize drugs more slowly and to be more sensitive to side effects of drugs. A single-dose pharmacokinetic y demonstrated that the disposition of bupropion and metabolites in elderly subjects was similar to that of nger subjects (see CLINICAL PHARMACOLOGY). Of approximately 5,600 patients who participated in clini trials with bupropion sustained-release tablets (depres and smoking cessation studies), 303 were 60 to 69 years and 88 were 70 years of age or older. The experience patients 60 years of age or older was similar to that in nger patients.

VERSE REACTIONS

also WARNINGS and PRECAUTIONS)

information included under ADVERSE REACTIONS is d primarily on data from the dose-response trial and comparative trial that evaluated ZYBAN for smoking ation (see CLINICAL TRIALS). Information on addi al adverse events associated with the sustained-release ulation of bupropion in depression trials, as well as the ediate-release formulation of bupropion, is included in parate section (see Other Events Observed During the ical Development and Postmarketing Experience of Bu pion).

erse Events Associated With the Discontinuation of atment: Adverse events were sufficiently troublesome ause discontinuation of treatment in 8% of the 706 pa nts treated with ZYBAN and 5% of the 313 patients ted with placebo. The more common events leading to ntinuation of treatment with ZYBAN included nervous tem disturbances (3.4%), primarily tremors, and skin rders (2.4%), primarily rashes.

dence of Commonly Observed Adverse Events: The st commonly observed adverse events consistently asso ed with the use of ZYBAN were dry mouth and insom . The most commonly observed adverse events were de d as those that consistently occurred at a rate of five per tage points greater than that for placebo across clinical dies.

e Dependency of Adverse Events: The incidence of mouth and insomnia may be related to the dose of BAN. The occurrence of these adverse events may be imized by reducing the dose of ZYBAN. In addition, in nia may be minimized by avoiding bedtime doses.

verse Events Occurring at an Incidence of 1% or More ong Patients Treated With ZYBAN: Table 3 enumer s selected treatment-emergent adverse events from the e-response trial that occurred at an incidence of 1% or re and were more common in patients treated with BAN compared to those treated with placebo. Table 4 imerates selected treatment-emergent adverse events m the comparative trial that occurred at an incidence of or more and were more common in patients treated with BAN, NTS, or the combination of ZYBAN and NTS com red to those treated with placebo. Reported adverse nts were classified using a COSTART-based dictionary

Table 3: Treatment-Emergent Adverse Event Incidence in the Dose-Response Trial*

Body System/ Adverse Experience	ZYBAN† 100 to 300 mg/day (n = 461) %	Placebo (n = 150) %
dy (General)		
leck pain	2	<1
llergic reaction	1	0
rdiovascular		
lot flashes	1	0
lypertension	1	<1
gestive		
ry mouth	11	5
ncreased appetite	2	<1
norexia	1	<1
sculoskeletal		
rthralgia	4	3
lyalgia	2	1
rvous system		
nsomnia	31	21
izziness	8	7
remor	2	1
omnolence	2	1
moking abnormality	1	0
spiratory		
ronchitis	2	0
Skin		
Pruritus	3	<1
Rash	3	<1
Dry skin	2	0
Urticaria	1	0
Special senses		
Taste perversion	2	<1

*Selected adverse events with an incidence of at least 1% of patients treated with ZYBAN and more frequent than in the placebo group.

[See table 4 at top of next page)

Other Events Observed During the Clinical Development and Postmarketing Experience of Bupropion: In addition to the adverse events noted above, the following events have been reported in clinical trials with the sustained-release formulation of bupropion in depressed patients and in non-depressed smokers, as well as in clinical trials and postmarketing clinical experience with the immediate-release formulation of bupropion.

Adverse events for which frequencies are provided below occurred in clinical trials with bupropion sustained-release. The frequencies represent the proportion of patients who experienced a treatment-emergent adverse event on at least one occasion in placebo-controlled studies for depression (n=987) or smoking cessation (n=1,013), or patients who experienced an adverse event requiring discontinuation of treatment in an open-label surveillance study with bupropion sustained-release tablets (n=3,100). All treatment-emergent adverse events are included except those listed in Tables 3 and 4, those events listed in other safety-related sections of the insert, those adverse events subsumed under COSTART terms that are either overly general or excessively specified so as to be uninformative, those events not reasonably associated with the use of the drug, and those events that were not serious and occurred in fewer than two patients.

Events are further categorized by body system and listed in order of decreasing frequency according to the following definitions of frequency: Frequent adverse events are defined as those occurring in at least 1/100 patients. Infrequent adverse events are those occurring in 1/100 to 1/1,000 patients, while rare events are those occurring in less than 1/1,000 patients.

Adverse events for which frequencies are not provided occurred in clinical trials or postmarketing experience with the immediate-release formulation of bupropion. Only those adverse events not previously listed for sustained-release bupropion are included. The extent to which these events may be associated with ZYBAN is unknown.

Body (General): Frequent were asthenia, fever, and headache. Infrequent were back pain, chills, inguinal hernia, musculoskeletal chest pain, pain, and photosensitivity. Rare was malaise.

Cardiovascular: Infrequent were flushing, migraine, postural hypotension, stroke, tachycardia, and vasodilation. Rare was syncope. Also observed were cardiovascular disorder, complete AV block, extrasystoles, hypotension, myocardial infarction, phlebitis, and pulmonary embolism.

Digestive: Frequent were dyspepsia, flatulence, and vomiting. Infrequent were abnormal liver function, bruxism, dysphagia, gastric reflux, gingivitis, glossitis, jaundice, and stomatitis. Rare was edema of tongue. Also observed were colitis, esophagitis, gastrointestinal hemorrhage, gum hemorrhage, hepatitis, increased salivation, intestinal perforation, liver damage, pancreatitis, stomach ulcer, and stool abnormality.

Endocrine: Also observed was syndrome of inappropriate antidiuretic hormone.

Hemic and Lymphatic: Infrequent was ecchymosis. Also observed were anemia, leukocytosis, leukopenia, lymphadenopathy, and pancytopenia.

Metabolic and Nutritional: Infrequent were edema, increased weight, and peripheral edema. Also observed was glycosuria.

Musculoskeletal: Infrequent were leg cramps and twitching. Also observed were arthritis and muscle rigidity/fever/rhabdomyolysis.

Nervous System: Frequent were agitation, depression, and irritability. Infrequent were abnormal coordination, CNS stimulation, confusion, decreased libido, decreased memory, depersonalization, emotional lability, hostility, hyperkinesia, hypertonia, hypesthesia, paresthesia, suicidal ideation, and vertigo. Rare were amnesia, ataxia, derealization, and hypomania. Also observed were abnormal electroencephalogram (EEG), akinesia, aphasia, coma, delirium, delusions, dysarthria, dyskinesia, dystonia, euphoria, extrapyramidal syndrome, hypokinesia, increased libido, manic reaction, neuralgia, neuropathy, paranoid reaction, and unmasking tardive dyskinesia.

Respiratory: Rare was bronchospasm. Also observed was pneumonia.

Skin: Frequent was sweating. Infrequent was acne and dry skin. Rare was maculopapular rash. Also observed were angioedema, exfoliative dermatitis, and hirsutism.

Special Senses: Frequent was amblyopia. Infrequent were accommodation abnormality and dry eye. Also observed were deafness, diplopia, and mydriasis.

Urogenital: Frequent was urinary frequency. Infrequent were impotence, polyuria, and urinary urgency. Also observed were abnormal ejaculation, cystitis, dyspareunia, dysuria, gynecomastia, menopause, painful erection, prostate disorder, salpingitis, urinary incontinence, urinary retention, urinary tract disorder, and vaginitis.

DRUG ABUSE AND DEPENDENCE

ZYBAN is likely to have a low abuse potential.

Humans: There have been few reported cases of drug dependence and withdrawal symptoms associated with the immediate-release formulation of bupropion. In human studies of abuse liability, individuals experienced with drugs of abuse reported that bupropion produced a feeling of euphoria and desirability. In these subjects, a single dose of 400 mg (1.33 times the recommended daily dose) of bupropion produced mild amphetamine-like effects compared to placebo on the Morphine-Benzedrine Subscale of the Addiction Research Center Inventories (ARCI), which is indicative of euphorigenic properties and a score intermediate between placebo and amphetamine on the Liking Scale of the ARCI.

Animals: Studies in rodents and primates have shown that bupropion exhibits some pharmacologic actions common to psychostimulants. In rodents, it has been shown to increase locomotor activity, elicit a mild stereotyped behavioral response, and increase rates of responding in several schedule-controlled behavior paradigms. In primate models to assess the positive reinforcing effects of psychoactive drugs, bupropion was self-administered intravenously. In rats, bupropion produced amphetamine- and cocaine-like discriminative stimulus effects in drug discrimination paradigms used to characterize the subjective effects of psychoactive drugs.

The possibility that bupropion may induce dependence should be kept in mind when evaluating the desirability of including the drug in smoking cessation programs of individual patients.

OVERDOSAGE

Human Overdose Experience: There has been very limited experience with overdosage of the sustained-release formulation of bupropion; three such cases were reported during clinical trials in depressed patients. One patient ingested 3,000 mg of bupropion sustained-release tablets and vomited quickly after the overdose; the patient experienced blurred vision and lightheadedness. A second patient ingested a "handful" of bupropion sustained-release tablets and experienced confusion, lethargy, nausea, jitteriness, and seizure. A third patient ingested 3,600 mg of bupropion sustained-release tablets and a bottle of wine; the patient experienced nausea, visual hallucinations, and "grogginess." None of the patients experienced further sequelae.

There has been extensive experience with overdosages of the immediate-release formulation of bupropion. Thirteen overdoses occurred during clinical trials in depressed patients. Twelve patients ingested 850 to 4,200 mg and recovered without significant sequelae. Another patient who ingested 9,000 mg of the immediate-release formulation of bupropion and 300 mg of tranylcypromine experienced a grand mal seizure and recovered without further sequelae.

Since introduction, overdoses of up to 17,500 mg of the immediate-release formulation of bupropion have been reported. Seizure was reported in approximately one third of all cases. Other serious reactions reported with overdoses of the immediate-release formulation of bupropion alone included hallucinations, loss of consciousness, and sinus tachycardia. Fever, muscle rigidity, rhabdomyolysis, hypotension, stupor, coma, and respiratory failure have been reported when the immediate-release formulation of bupropion was part of multiple drug overdoses.

Although most patients recovered without sequelae, deaths associated with overdoses of the immediate-release formulation of bupropion alone have been reported rarely in patients ingesting massive doses of the drug. Multiple uncontrolled seizures, bradycardia, cardiac failure, and cardiac arrest prior to death were reported in these patients.

Management of Overdose: Following suspected overdose, hospitalization is advised. If the patient is conscious, vomiting should be induced by syrup of ipecac. Activated charcoal also may be administered every 6 hours during the first 12 hours after ingestion. Baseline laboratory values should be obtained. Electrocardiogram and EEG monitoring also are recommended for the next 48 hours. Adequate fluid intake should be provided.

If the patient is stuporous, comatose, or convulsing, airway intubation is recommended prior to undertaking gastric lavage. Although there is little clinical experience with lavage following an overdose of bupropion, it is likely to be of benefit within the first 12 hours after ingestion since absorption of the drug may not yet be complete.

Table 4: Treatment-Emergent Adverse Event Incidence in the Comparative Trial*

Adverse Experience (COSTART Term)	ZYBAN™ 300 mg/day (n = 243) %	Nicotine Transdermal System (NTS) 21 mg/day (n = 243) %	ZYBAN and NTS (n = 244) %	Placebo (n = 159) %
Body				
Abdominal pain	3	4	1	1
Accidental injury	2	2	1	1
Chest pain	<1	1	3	1
Neck pain	2	1	<1	0
Facial edema	<1	0	1	0
Cardiovascular				
Hypertension	1	<1	2	0
Palpitations	2	0	1	0
Digestive				
Nausea	9	7	11	4
Dry mouth	10	4	9	4
Constipation	8	4	9	3
Diarrhea	4	4	3	1
Anorexia	3	1	5	1
Mouth ulcer	2	1	1	1
Thirst	<1	<1	2	0
Musculoskeletal				
Myalgia	4	3	5	3
Arthralgia	5	3	3	2
Nervous system				
Insomnia	40	28	45	18
Dream abnormality	5	18	13	3
Anxiety	8	6	9	6
Disturbed concentration	9	3	9	4
Dizziness	10	2	8	6
Nervousness	4	<1	2	2
Tremor	1	<1	2	0
Dysphoria	<1	1	2	1
Respiratory				
Rhinitis	12	11	9	8
Increased cough	3	5	<1	1
Pharyngitis	3	2	3	0
Sinusitis	2	2	2	1
Dyspnea	1	0	2	1
Epistaxis	2	1	1	0
Skin				
Application site reaction†	11	17	15	7
Rash	4	3	3	2
Pruritus	3	1	5	1
Urticaria	2	0	2	0
Special Senses				
Taste perversion	3	1	3	2
Tinnitus	1	0	<1	0

*Selected adverse events with an incidence of at least 1% of patients treated with either ZYBAN, NTS, or the combination of ZYBAN and NTS and more frequent than in the placebo group.
†Patients randomized to ZYBAN or placebo received placebo patches.

While diuresis, dialysis, or hemoperfusion are sometimes used to treat drug overdosage, there is no experience with their use in the management of overdoses of bupropion. Because diffusion of bupropion and its metabolites from tissue to plasma may be slow, dialysis may be of minimal benefit. Based on studies in animals, it is recommended that seizures be treated with an intravenous benzodiazepine preparation and other supportive measures, as appropriate. Further information about the treatment of overdoses may be available from a poison control center.

DOSAGE AND ADMINISTRATION

ZYBAN: ***Usual Dosage for Adults:*** The recommended and maximum dose of ZYBAN is 300 mg/day, given as 150 mg twice daily. Dosing should begin at 150 mg/day given every day for the first 3 days, followed by a dose increase for most patients to the recommended usual dose of 300 mg/day. There should be an interval of at least 8 hours between successive doses. Doses above 300 mg/day should not be used (see WARNINGS). Treatment with ZYBAN should be initiated **while the patient is still smoking,** since approximately 1 week of treatment is required to achieve steady-state blood levels of bupropion. Patients should set a "target quit date" within the first 2 weeks of treatment with ZYBAN, generally in the second week. Treatment with ZYBAN should be continued for 7 to 12 weeks; duration of treatment should be based on the relative benefits and risks for individual patients. If a patient has not made significant progress towards abstinence by the seventh week of therapy with ZYBAN, it is unlikely that he or she will quit during that attempt, and treatment should probably be discontinued. Dose tapering of ZYBAN is not required when discontinuing treatment. It is important that patients continue to receive counseling and support throughout treatment with ZYBAN, and for a period of time thereafter.

Individualization of Therapy: Patients are more likely to quit smoking and remain abstinent if they are seen frequently and receive support from their physicians or other health care professionals. It is important to ensure that patients read the instructions provided to them and have their questions answered. Physicians should review the patient's overall smoking cessation program that includes treatment with ZYBAN. Patients should be advised of the importance of participating in the behavioral interventions, counseling, and/or support services to be used in conjunction with ZYBAN. See information for patients at the end of the package insert.

The goal of therapy with ZYBAN is complete abstinence. If a patient has not made significant progress towards abstinence by the seventh week of therapy with ZYBAN, it is unlikely that he or she will quit during that attempt, and treatment should be discontinued.

Patients who fail to quit smoking during an attempt may benefit from interventions to improve their chances for success on subsequent attempts. Patients who are unsuccessful should be evaluated to determine why they failed. A new quit attempt should be encouraged when factors that contributed to failure can be eliminated or reduced, and conditions are more favorable.

Maintenance: Although clinical data are not available regarding the long-term use (>12 weeks) of bupropion for smoking cessation, bupropion has been used for longer periods of time in the treatment of depression. Whether to continue treatment with ZYBAN for periods longer than 12 weeks for smoking cessation must be determined for individual patients.

Combination Treatment With ZYBAN and a Nicotine Transdermal System (NTS): Combination treatment with ZYBAN and NTS may be prescribed for smoking cessation. The prescriber should review the complete prescribing information for both ZYBAN and NTS before using combination treatment. See also CLINICAL TRIALS for met and dosing used in the ZYBAN and NTS combination t Monitoring for treatment-emergent hypertension in tients treated with the combination of ZYBAN and NT recommended.

HOW SUPPLIED

ZYBAN Sustained-Release Tablets, 150 mg of bupropion drochloride, are purple, round, biconvex, film-coated tal printed with "ZYBAN 150" in bottles of 60 (NDC 0173-0 02) tablets and the ZYBAN Advantage Pack™ containi bottle of 60 (NDC 0173-0556-01) tablets.

Store at controlled room temperature, 20° to 25°C (68 77°F) (see USP). Dispense in tight, light-resistant cont ers as defined in the USP.

PATIENT INFORMATION: The following wordin contained in a separate leaflet provided for patients.

Information for the Patient

ZYBAN™ (bupropion hydrochloride) Sustained-Rele Tablets

Please read this information before you start tak ZYBAN. Also read this leaflet each time you renew your scription, in case anything has changed. This informatio not intended to take the place of discussions between and your doctor. You and your doctor should discuss ZYB as part of your plan to stop smoking. Your doctor has scribed ZYBAN for your use only. Do not let anyone else your ZYBAN.

IMPORTANT WARNING:

There is a chance that approximately 1 out of every 1, people taking bupropion hydrochloride, the active ingre ent in ZYBAN, will have a seizure. The chance of this h pening increases if you:

- have a seizure disorder (for example, epilepsy);
- have or have had an eating disorder (for example, bulir or anorexia nervosa);
- take more than the recommended amount of ZYBAN;
- take other medicines with the same active ingredient t is in ZYBAN, such as WELLBUTRIN® (bupropion hyd chloride) Tablets and WELLBUTRIN® SR (bupropion drochloride) Sustained-Release Tablets. (Both of th medicines are used to treat depression.)

You can reduce the chance of experiencing a seizure by lowing your doctor's directions on how to take ZYBAN. should also discuss with your doctor whether ZYBAN right for you.

1. What is ZYBAN?

ZYBAN is a prescription medicine to help people quit sm ing. Studies have shown that more than one third of peo quit smoking for at least 1 month while taking ZYBAN a participating in a patient support program. For many tients, ZYBAN reduces withdrawal symptoms and the u to smoke. ZYBAN should be used with a patient supp program. It is important to participate in the behavio program, counseling, or other support program your hea care professional recommends.

2. Who should not take ZYBAN?

You should not take ZYBAN if you:

- have a seizure disorder (for example, epilepsy).
- are already taking WELLBUTRIN, WELLBUTRIN SR, any other medicines that contain bupropion hydroch ride.
- have or have had an eating disorder (for example, bulir or anorexia nervosa).
- are currently taking or have recently taken a monoami oxidase inhibitor (MAOI).
- are allergic to bupropion.

3. Are there special concerns for women?

ZYBAN is not recommended for women who are pregnant breast-feeding. Women should notify their doctor if they b come pregnant or intend to become pregnant while taki ZYBAN.

4. How should I take ZYBAN?

- You should take ZYBAN as directed by your doctor. Tl usual recommended dosing is to take one 150-mg tablet the morning for the first 3 days. On the fourth day, beg taking one 150-mg tablet in the morning and one 150-m tablet in the early evening. Doses should be taken at lea 8 hours apart.
- **Never take an "extra" dose of ZYBAN.** If you forget take a dose, do not take an extra tablet to "catch up" f the dose you forgot. Wait and take your next tablet at t regular time. Do not take more tablets than your doct prescribed. This is important so you do not increase yo chance of having a seizure.
- It is important to swallow ZYBAN Tablets whole. Do n chew, divide, or crush tablets.

Continued on next page

This product information is based on labeling in effect on Jun 1, 1998. For further information, contact via direct mail, phon or web site Medical Information: Glaxo Wellcome Inc., PO B 13398, Research Triangle Park, NC 27709. Healthca Professionals (Medical Information): 800-334-0089 Patien (Customer Response Center): 888-TALK2GW (1-888-825-524 Glaxo Wellcome Corporate Web Site: www.glaxowellcome.co

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How long should I take ZYBAN?
ost people should take ZYBAN for 7 to 12 weeks. Follow ur doctor's instructions.

When should I stop smoking?
takes about 1 week for ZYBAN to reach the right levels in ur body to be effective. So, to maximize your chance of itting, you should not stop smoking until you have been king ZYBAN for 1 week. You should set a date to stop oking during the second week you're taking ZYBAN.

Can I smoke while taking ZYBAN?
is not physically dangerous to smoke and use ZYBAN at e same time. However, continuing to smoke after the date u set to stop smoking will seriously reduce your chance of eaking your smoking habit.

Can ZYBAN be used at the same time as nicotine patches?
s, ZYBAN and nicotine patches can be used at the same ne but should only be used together under the supervision your doctor. Using ZYBAN and nicotine patches together ay raise your blood pressure. Your doctor will probably ant to check your blood pressure regularly to make sure at it stays within acceptable levels.

O NOT SMOKE AT ANY TIME if you are using a nicotine tch or any other nicotine product along with ZYBAN. It is ssible to get too much nicotine and have serious side ef cts.

What are possible side effects of ZYBAN?
ke all medicines, ZYBAN may cause side effects. The most common side effects include dry mouth and dif ficulty sleeping. These side effects are generally mild and often disappear after a few weeks. If you have difficulty sleeping, avoid taking your medicine too close to bedtime. The most common side effects that caused people to stop taking ZYBAN during clinical studies were shakiness and skin rash.

Contact your doctor or health care professional if you have a rash or other troublesome side effects.

Use caution before driving a car or operating complex, hazardous machinery until you know if ZYBAN affects your ability to perform these tasks.

Can I drink alcohol while I am taking ZYBAN?
is best to not drink alcohol at all or to drink very little hile taking ZYBAN. If you drink a lot of alcohol and sud enly stop, you may increase your chance of having a sei ure. Therefore, it is important to discuss your use of alco ol with your doctor before you begin taking ZYBAN.

Will ZYBAN affect other medicines I am taking?
YBAN may affect other medicines you're taking. It is im ortant not to take medicines that may increase the chance r you to have a seizure. Therefore, you should make sure at your doctor knows about all medicines—prescription or ver-the-counter—you are taking or plan to take.

Do ZYBAN Tablets have a characteristic odor?
YBAN Tablets may have a characteristic odor. If present, is odor is normal.

How should I store ZYBAN?
Store ZYBAN at room temperature, out of direct sunlight. Keep ZYBAN in a tightly closed container.

Keep ZYBAN out of the reach of children.

his summary provides important information about YBAN. This summary cannot replace the more detailed in rmation that you need from your doctor. If you have any uestions or concerns about either ZYBAN or smoking ces ation, talk to your doctor or other health care professional.

[ABITROL is a registered trademark of Ciba-Geigy Corporation]

U.S. Patent Nos. 5,427,798 and 5,358,970

eptember 1997/RL-448

Shown in Product Identification Guide, page 315

YLOPRIM ® R
r 15-prim]
llopurinol)
00 mg Scored Tablets and
00 mg Scored Tablets

ESCRIPTION

YLOPRIM (allopurinol) is known chemically as 1,5-dihy ro-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one. It is a xanthine ox ase inhibitor which is administered orally. Each scored hite tablet contains 100 mg allopurinol and the inactive gredients lactose, magnesium stearate, potato starch, and ovidone. Each scored peach tablet contains 300 mg allopu ol and the inactive ingredients corn starch, FD&C Yellow No. 6 Lake, lactose, magnesium stearate, and povidone. Its solubility in water at 37°C is 80.0 mg/dL and is greater in an alkaline solution.

CLINICAL PHARMACOLOGY

ZYLOPRIM acts on purine catabolism, without disrupting the biosynthesis of purines. It reduces the production of uric acid by inhibiting the biochemical reactions immediately preceding its formation.

ZYLOPRIM is a structural analogue of the natural purine base, hypoxanthine. It is an inhibitor of xanthine oxidase, the enzyme responsible for the conversion of hypoxanthine to xanthine and of xanthine to uric acid, the end product of purine metabolism in man. ZYLOPRIM is metabolized to the corresponding xanthine analogue, oxipurinol (alloxanthine), which also is an inhibitor of xanthine oxidase.

It has been shown that reutilization of both hypoxanthine and xanthine for nucleotide and nucleic acid synthesis is markedly enhanced when their oxidations are inhibited by ZYLOPRIM and oxipurinol. This reutilization does not disrupt normal nucleic acid anabolism, however, because feedback inhibition is an integral part of purine biosynthesis. As a result of xanthine oxidase inhibition, the serum concentration of hypoxanthine plus xanthine in patients receiving ZYLOPRIM for treatment of hyperuricemia is usually in the range of 0.3 to 0.4 mg/dL compared to a normal level of approximately 0.15 mg/dL. A maximum of 0.9 mg/dL of these oxypurines has been reported when the serum urate was lowered to less than 2 mg/dL by high doses of ZYLOPRIM. These values are far below the saturation levels at which point their precipitation would be expected to occur (above 7 mg/dL).

The renal clearance of hypoxanthine and xanthine is at least 10 times greater than that of uric acid. The increased xanthine and hypoxanthine in the urine have not been accompanied by problems of nephrolithiasis. Xanthine crystalluria has been reported in only three patients. Two of the patients had Lesch-Nyhan syndrome, which is characterized by excessive uric acid production combined with a deficiency of the enzyme, hypoxanthineguanine phosphoribosyltransferase (HGPRTase). This enzyme is required for the conversion of hypoxanthine, xanthine, and guanine to their respective nucleotides. The third patient had lymphosarcoma and produced an extremely large amount of uric acid because of rapid cell lysis during chemotherapy.

ZYLOPRIM is approximately 90% absorbed from the gastrointestinal tract. Peak plasma levels generally occur at 1.5 hours and 4.5 hours for ZYLOPRIM and oxipurinol respectively, and after a single oral dose of 300 mg ZYLOPRIM, maximum plasma levels of about 3 mcg/mL of ZYLOPRIM and 6.5 mcg/mL of oxipurinol are produced.

Approximately 20% of the ingested ZYLOPRIM is excreted in the feces. Because of its rapid oxidation to oxipurinol and a renal clearance rate approximately that of glomerular filtration rate, ZYLOPRIM has a plasma half-life of about 1 to 2 hours. Oxipurinol, however, has a longer plasma half-life (approximately 15 hours) and therefore effective xanthine oxidase inhibition is maintained over a 24-hour period with single daily doses of ZYLOPRIM. Whereas ZYLOPRIM is cleared essentially by glomerular filtration, oxipurinol is reabsorbed in the kidney tubules in a manner similar to the reabsorption of uric acid.

The clearance of oxipurinol is increased by uricosuric drugs, and as a consequence, the addition of a uricosuric agent reduces to some degree the inhibition of xanthine oxidase by oxipurinol and increases to some degree the urinary excretion of uric acid. In practice, the net effect of such combined therapy may be useful in some patients in achieving minimum serum uric acid levels provided the total urinary uric acid load does not exceed the competence of the patient's renal function.

Hyperuricemia may be primary, as in gout, or secondary to diseases such as acute and chronic leukemia, polycythemia vera, multiple myeloma, and psoriasis. It may occur with the use of diuretic agents, during renal dialysis, in the presence of renal damage, during starvation or reducing diets, and in the treatment of neoplastic disease where rapid resolution of tissue masses may occur. Asymptomatic hyperuricemia is not an indication for treatment with ZYLOPRIM (see INDICATIONS AND USAGE).

Gout is a metabolic disorder which is characterized by hyperuricemia and resultant deposition of monosodium urate in the tissues, particularly the joints and kidneys. The etiology of this hyperuricemia is the overproduction of uric acid in relation to the patient's ability to excrete it. If progressive deposition of urates is to be arrested or reversed, it is necessary to reduce the serum uric acid level below the saturation point to suppress urate precipitation.

Administration of ZYLOPRIM generally results in a fall in both serum and urinary uric acid within 2 to 3 days. The degree of this decrease can be manipulated almost at will since it is dose-dependent. A week or more of treatment with ZYLOPRIM may be required before its full effects are manifested; likewise, uric acid may return to pretreatment levels slowly (usually after a period of 7 to 10 days following cessation of therapy). This reflects primarily the accumulation and slow clearance of oxipurinol. In some patients a dramatic fall in urinary uric acid excretion may not occur, particularly in those with severe tophaceous gout. It has been postulated that this may be due to the mobilization of urate from tissue deposits as the serum uric acid level begins to fall.

The action of ZYLOPRIM differs from that of uricosuric agents, which lower the serum uric acid level by increasing urinary excretion of uric acid. ZYLOPRIM reduces both the serum and urinary uric acid levels by inhibiting the formation of uric acid. The use of ZYLOPRIM to block the formation of urates avoids the hazard of increased renal excretion of uric acid posed by uricosuric drugs.

ZYLOPRIM can substantially reduce serum and urinary uric acid levels in previously refractory patients even in the presence of renal damage serious enough to render uricosuric drugs virtually ineffective. Salicylates may be given conjointly for their antirheumatic effect without compromising the action of ZYLOPRIM. This is in contrast to the nullifying effect of salicylates on uricosuric drugs.

ZYLOPRIM also inhibits the enzymatic oxidation of mercaptopurine, the sulfur-containing analogue of hypoxanthine, to 6-thiouric acid. This oxidation, which is catalyzed by xanthine oxidase, inactivates mercaptopurine. Hence, the inhibition of such oxidation by ZYLOPRIM may result in as much as a 75% reduction in the therapeutic dose requirement of mercaptopurine when the two compounds are given together.

INDICATIONS AND USAGE

THIS IS NOT AN INNOCUOUS DRUG. IT IS NOT RECOMMENDED FOR THE TREATMENT OF ASYMPTOMATIC HYPERURICEMIA.

ZYLOPRIM reduces serum and urinary uric acid concentrations. Its use should be individualized for each patient and requires an understanding of its mode of action and pharmacokinetics (see CLINICAL PHARMACOLOGY, CONTRAINDICATIONS, WARNINGS and PRECAUTIONS).

ZYLOPRIM is indicated in:

(1) the management of patients with signs and symptoms of primary or secondary gout (acute attacks, tophi, joint destruction, uric acid lithiasis and/or nephropathy).

(2) the management of patients with leukemia, lymphoma and malignancies who are receiving cancer therapy which causes elevations of serum and urinary uric acid levels. Treatment with ZYLOPRIM should be discontinued when the potential for overproduction of uric acid is no longer present.

(3) the management of patients with recurrent calculiform calculi whose daily uric acid excretion exceeds 800 mg/day in male patients and 750 mg/day in female patients. Therapy in such patients should be carefully assessed initially and reassessed periodically to determine in each case that treatment is beneficial and that the benefits outweigh the risks.

CONTRAINDICATIONS

Patients who have developed a severe reaction to ZYLOPRIM should not be restarted on the drug.

WARNINGS

ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR OTHER SIGNS WHICH MAY INDICATE AN ALLERGIC REACTION. In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial, and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme exudativum), and/or generalized vasculitis, irreversible hepatotoxicity and on rare occasions death.

In patients receiving PURINETHOL® (mercaptopurine) or IMURAN® (azathioprine), the concomitant administration of 300 to 600 mg of ZYLOPRIM per day will require a reduction in dose to approximately one third to one fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of mercaptopurine or azathioprine should be made on the basis of therapeutic response and the appearance of toxic effects (see CLINICAL PHARMACOLOGY).

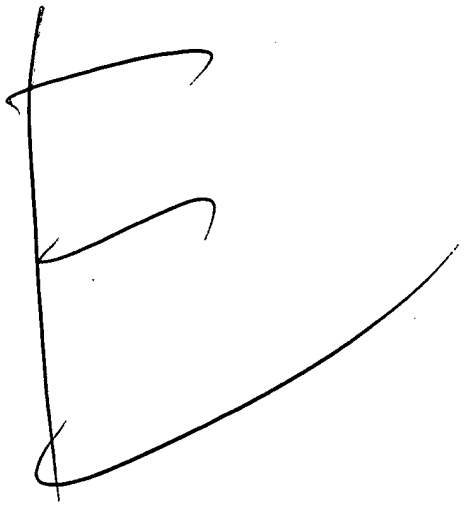
A few cases of reversible clinical hepatotoxicity have been noted in patients taking ZYLOPRIM, and in some patients, asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. If anorexia, weight loss, or pruritus develop in patients on ZYLOPRIM, evaluation of liver function should be part of their diagnostic workup. In patients with pre-existing liver disease, periodic liver function tests are recommended during the early stages of therapy.

Due to the occasional occurrence of drowsiness, patients should be alerted to the need for due precaution when engaging in activities where alertness is mandatory.

The occurrence of hypersensitivity reactions to ZYLOPRIM may be increased in patients with decreased renal function receiving thiazides and ZYLOPRIM concurrently. For this reason, in this clinical setting, such combinations should be administered with caution and patients should be observed closely.

PRECAUTIONS

General: An increase in acute attacks of gout has been reported during the early stages of administration of



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UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/427,447	10/27/1999	ALEXANDER GOEN SZYNALSKI		3197

7590 12/04/2001

MARK POHL
55 MADISON AVENUE, 4TH FLOOR
MORRISTOWN, NJ 07960

EXAMINER	
RIMELL, SAMUEL G	
ART UNIT	**PAPER NUMBER**
2166	

DATE MAILED: 12/04/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/427,447	SZYNALSKI, ALEXANDER GOEN	
	Examiner	Art Unit	
	Sam Rimell	2166	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,11 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 11 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Sam Rimell
Primary Examiner
AU 2166

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1, 11 and 21-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1 and 11 have been amended to recite the usage of an "anti-smoking drug" instead of the originally recited "Lobelia".

The term "anti-smoking drug" broader in scope than the recitations of Lobelia found in the disclosure. Since the term "anti-smoking drug" can encompass prescription pharmaceuticals, it is far broader in scope than the recitation of Lobelia found in the disclosure.

Claims 1 and 11 can be corrected by deploying the term "Lobelia". This may be accomplished by Examiner's Amendment, with applicant's authorization.

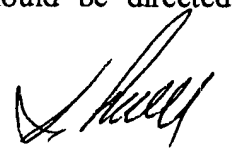
Claim 1, 11 and 21-24 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112, first paragraph, set forth in this Office action.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

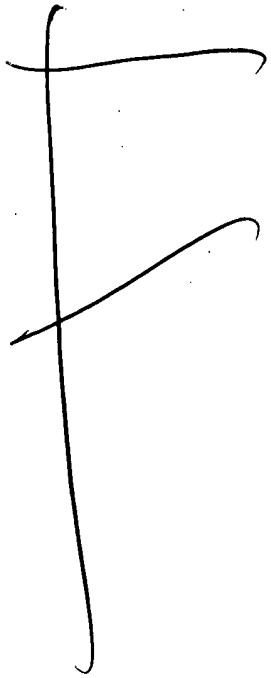
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication should be directed to Sam Rimell at telephone number (703) 306-5626.



Sam Rimell
Primary Examiner
Art Unit 2166



Interview Summary	Application No.	Applicant(s)	
	09/427,447	SZYNALSKI, ALEXANDER GOEN	
	Examiner	Art Unit	
	Sam Rimell	2166	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Sam Rimell*. (3)_____.

(2) *Mark Pohl*. (4)_____.

Date of Interview: *14 December 2001* .

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____ .

Claim(s) discussed: _____ .

Identification of prior art discussed: _____ .

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *Agreed to Examiner's Amendment to place application in condition for allowance* .

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

i)☐ It is not necessary for applicant to provide a separate record of the substance of the interview(if box is checked).

Unless the paragraph above has been checked, THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirements

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case unless both applicant and examiner agree that the examiner will record same. Where the examiner agrees to record the substance of the interview, or when it is adequately recorded on the Form or in an attachment to the Form, the examiner should check the appropriate box at the bottom of the Form which informs the applicant that the submission of a separate record of the substance of the interview as a supplement to the Form is not required.

It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Notice of Allowability	Application No.	Applicant(s)	
	09/427,447	SZYNALSKI, ALEXANDER GOEN	
	Examiner	Art Unit	
	Sam Rimell	2166	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to *Interview of 12/14/01*.
2. ☒ The allowed claim(s) is/are *1 and 11*.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☒ Notice of References Cited (PTO-892)
2☐ Notice of Informal Patent Application (PTO-152)
3☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
4☒ Interview Summary (PTO-413), Paper No.____ .
5☐ Information Disclosure Statements (PTO-1449), Paper No. ____.
6☒ Examiner's Amendment/Comment
7☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
8☒ Examiner's Statement of Reasons for Allowance
9☐ Other

SAM RIMELL
PRIMARY EXAM
AU 2166

Examiner's Amendment

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mark Pohl on 12/14/01.

In claim 1: In part C, change "an anti-smoking drug" to --lobelia--.

In claim 11: In part C, change "an anti-smoking drug" to --lobelia--.

Claims 21-24: These claims are cancelled.

Terminal Disclaimer

The present application includes a terminal disclaimer which appears to have been mis-directed to this application. The terminal disclaimer has been refused entry for the present application and will be transferred to a continuation application of the present case. No terminal disclaimer has been required for this application.

Reasons for Allowance

The present application includes two independent claims, 1 and 11. The closest prior art are the US Patents 5,414,005 to Schneider et al. and 5,055,478 to Cooper et al.

Schneider et al. differs from both claims 1 and 11 in that it does not disclose the usage of an educational program in combination with the usage of lobelia. Schneider et al. is primarily addressed to a sublingual form of lobelia with certain specified advantages.

Copper et al. differs from both claims 1 and 11 in that it does not disclose the combination of a non-conditioning educational program, a hypnosis program and lobelia administration.

Any inquiry concerning this communication should be directed to Sam Rimell at telephone number (703) 306-5626.

Sam Rimell
Primary Examiner
Art Unit 2166

Notice of References Cited	Application/Control No. 09/427,447	Applicant(s)/Patent Under Reexamination SZYNALSKI, ALEXANDER GOEN	
	Examiner Sam Rimell	Art Unit 2166	Page 1 of 1

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification	
	A	US-5055478	10-1991	Cooper et al.	514	343
	B	US-				
	C	US-				
	D	US-				
	E	US-				
	F	US-				
	G	US-				
	H	US-				
	I	US-				
	J	US-				
	K	US-				
	L	US-				
	M	US-				

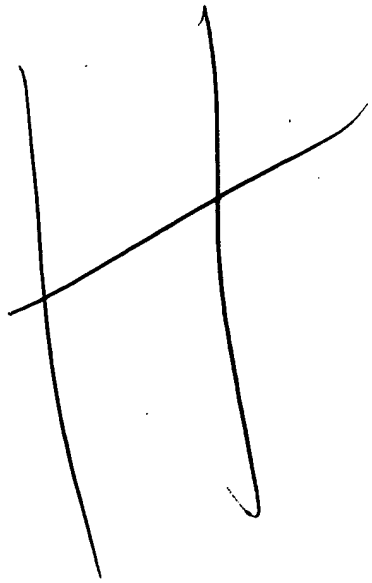
FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification	
	N						
	O						
	P						
	Q						
	R						
	S						
	T						

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/427,447	10/27/1999	ALEXANDER GOEN SZYNALSKI		3197

7590 02/04/2002

MARK POHL
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EXAMINER
RIMELL, SAMUEL G

ART UNIT	PAPER NUMBER
2166	

DATE MAILED: 02/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

CORRECTED **Notice of Allowability**	**Application No.** 09/427,447	**Applicant(s)** SZYNALSKI, ALEXANDER GOEN
	Examiner Sam Rimell	**Art Unit** 2166

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTOL-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☐ This communication is responsive to _____.
2. ☒ The allowed claim(s) is/are *1, 6, 11, 16*.
3. ☐ The drawings filed on _____ are accepted by the Examiner.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
   a) ☐ All b) ☐ Some* c) ☐ None of the:
      1. ☐ Certified copies of the priority documents have been received.
      2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
      3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

   * Certified copies not received: _____.
5. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
   (a) ☐ The translation of the foreign language provisional application has been received.
6. ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE**

7. ☐ A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.

8. ☐ CORRECTED DRAWINGS must be submitted.
   (a) ☐ including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
      1) ☐ hereto or 2) ☐ to Paper No. ____.
   (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the Examiner.
   (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

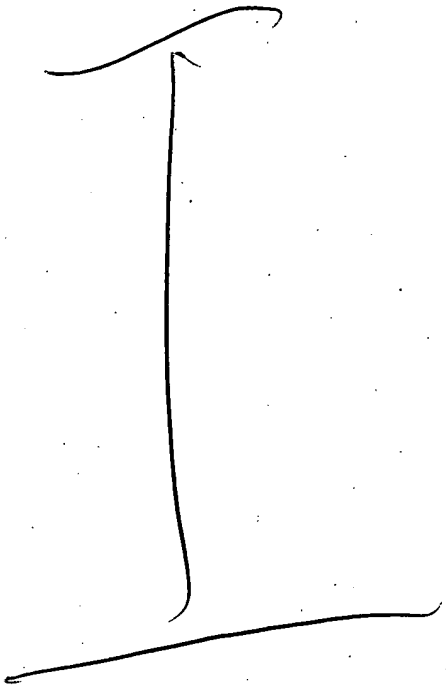
Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the top margin (not the back) of each sheet. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

9. ☐ DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1☐ Notice of References Cited (PTO-892)
3☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
5☐ Information Disclosure Statements (PTO-1449), Paper No. ____.
7☐ Examiner's Comment Regarding Requirement for Deposit of Biological Material
2☐ Notice of Informal Patent Application (PTO-152)
4☐ Interview Summary (PTO-413), Paper No.____ .
6☐ Examiner's Amendment/Comment
8☐ Examiner's Statement of Reasons for Allowance
9☐ Other

Sam Rimell
Primary Examiner
Art Unit: 2166



US006431874B1

(12) **United States Patent**
Szynalski

(10) **Patent No.: US 6,431,874 B1**
(45) **Date of Patent: Aug. 13, 2002**

(54) **STOP SMOKING METHOD AND COMPOSITION**

(75) Inventor: **Alexander Goen Szynalski**, Randolph, NJ (US)

(73) Assignee: **Goen Corporation**, Cedar Knolls, NJ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **09/427,447**

(22) Filed: **Oct. 27, 1999**

(51) **Int. Cl.**[7] **G09B 23/28**
(52) **U.S. Cl.** **434/262**
(58) **Field of Search** 514/282, 343; 424/449; 434/262

(56) **References Cited**

U.S. PATENT DOCUMENTS

5,055,478 A * 10/1991 Cooper et al. 514/343
5,414,005 A * 5/1995 Schneider et al. 514/343
5,780,051 A * 7/1998 Eswara et al. 424/449
5,965,567 A * 10/1999 Archer et al. 514/282

FOREIGN PATENT DOCUMENTS

GB 1017032 1/1966

* cited by examiner

Primary Examiner—Sam Rimell
(74) *Attorney, Agent, or Firm*—Pharmaceutical Patent Law, LLC; Mark Pohl

(57) **ABSTRACT**

The inventor discloses a unique, new and useful process to reduce tobacco smoking, entitled Stop Smoking Method and Composition, consisting of: (1) educating tobacco smokers regarding smoking, its physiological dangers and addictive nature, and techniques to stop smoking; (2) hypnotizing said tobacco smokers, and (3) providing dietary substances to address the nutritional needs of nicotine addiction and the nutritional challenges thereof.

8 Claims, No Drawings

STOP SMOKING METHOD AND COMPOSITION

BACKGROUND

The prior art discloses many stop-smoking products and methods including, for example; (A) education to educate smokers regarding smoking, its physiological dangers and addictive nature, and conscious techniques to stop smoking; (B) hypnosis, to use the unconscious mind to stop smoking; and (C) nutritional supplements, addressing the nutritional challenges with regard to stopping smoking.

SUMMARY

While using each one of these three elements is known in the art, I have found that by combining all of these three elements together, they act on the three areas most important for stopping smoking—the conscious mind, the unconscious mind, and the body—and are synergistically effective in helping people to stop smoking.

This synergy was unexpected. I am a Certified Hypnotist and am a Nutritionist, with over twenty years experience in the fields of hypnosis, seminar presentation and nutrition. I am a member of the American Association of Professional Hypnotherapists, the National Guild of Hypnotists, the International Association of Counselors and Therapists, and am certified by the Hypnodyne Foundation. I am listed in *Who's Who in Executives and Professionals*, and I was a finalist for the 1999 Ernst & Young Entrepreneur of the Year award. I have been a special guest on numerous national television and radio programs, and was featured on the #1 television fitness show in the country. I maintain a practice in Cedar Knolls, N.J. I have successfully used hypnosis in many types of situations. I have, for example, worked with athletes to improve their athletic performance, and have worked with corporations as a sales and personal-development trainer. I am driven by a sincere passion for helping people maximize their personal potential and overcome addictions to smoking and food. I enjoy a reputation for extremely high success through my seminars.

DETAILED DESCRIPTION

My invention therefore comprises three elements: (1) education for the conscious mind regarding smoking, its physiological dangers and addictive nature, and techniques to stop smoking; (2) hypnosis for the unconscious mind, which hypnosis addresses the unconscious mind and its way of affecting behavior; and (3) dietary substances, to address the physiological needs of a person entailed in stopping smoking.

Education. The first element of my invention is education regarding smoking. This educational process can include addressing the benefits of a regular exercise program. Thus, the educational materials or program educates the smoker to engage in some form of light exercise. Not only will exercise help clear the body of the toxins acquired through smoking, but exercise will also help release endorphins which relieve stress as well as making you feel good. Exercise will rapidly

reverse the damage done to the body from smoking. If the smoker has not engaged in exercise for a long time, or the smoker has a weight problem or any other health problem, the smoker should consult their physician before starting any regimen of exercise.

In addition to this, I have found that in my preferred embodiment of my invention, the education program also addresses the physiological progression of smoking, its physiological dangers and addictive nature, and some conscious techniques to stop smoking. ©1999

The physiological progression of smoking entails three discreet steps. Knowing these steps helps the smoker recognize them as they occur, and thus recognize the needs they fill.

Stage 1—Light a cigarette and inhale. This takes about 7 seconds. The deep breath of the inhale increases the flow of blood and oxygen to the heart and you feel more relaxed (not due to the cigarette, but due to the deep breath).

Stage 2—Seven seconds to fifteen minutes later, nicotine enters the liver, which in turn releases sugar into the bloodstream. This results in a physical uplift (not from the cigarette, but from the release of sugar into the bloodstream) which then in turn causes the pancreas to release insulin into the bloodstream. This gives you an energy boost. Normally, it is a temporary energy boost because the muscle cells of the body are resistant to insulin. So what happens is that your energy level goes up and then crashes, all over again. In fifteen minutes, you want to start smoking again due to the tense feelings you experience from your energy level being reduced. What we suggest is for you to sensitize your body to insulin. Before we suggest how you do this, you first should study the two diagrams pictured below. To better understand this phenomenon, we will provide an in-depth clarification of the diagrams.

Stage 3—Fifteen to twenty minutes after beginning to smoke, the nicotine interrupts the normal transmission of neurons by competing with acetylcholine at the nerve terminal, producing such effects as an increased heart rate and respiration, along with feelings of tension and of being "wired up." It also increases arousal and a sense of well-being and focused attention. A side benefit to understanding this step is to take proper nutrients so you do not allow this physical and physiological progression of smoking to occur. This will help with maintaining or even reducing weight and increasing lean muscle tissue.

In my preferred embodiment, the smoker is educated on the physiological dangers and addictive nature of smoking. These dangers are now so widely known as to not need to be discussed in detail here.

In my preferred embodiment, the person is educated on the benefits of modifying their daily diet. This addresses potential weight gain problems, one of the biggest fears of smokers.

Regarding potential weight gain, why do we gain weight when we stop smoking? Muscle cells become more sensitive to insulin. In my preferred embodiment, therefore, I recommend:

Avoid refined carbohydrates. All carbohydrates start out in their rarest edible form as complex, but we make them refined by processing, preserving, storing, drying, and cooking.

Increase physical activity, especially five to fifteen minutes after meals.

Take 100 micrograms of chromium along with the proper cofactors, one half hour before each meal with a full glass of water. The product containing chromium (CHROMIUM CHELAVITE™) that I prefer is TRIMSPA®, available from Vitamerica, Inc., Cedar Knolls, N.J.

Acquire a cigarette cessation product containing the herb lobelia, which aids any withdrawal that some may experience. Lobelia is a natural herb that tricks the body into thinking it is nicotine, but it does not have the side effects. In the preferred embodiment of my invention, I recommend CIGSATION™, available from Vitamerica, Inc., Cedar Knolls, N.J.

Cut back on drinking coffee and other caffeinated beverages. Sometimes the stress or anxiety that quitters experience is due to the physiological effects of caffeine on the nervous system and not due to withdrawal from nicotine. Try drinking decaffeinated tea or some other warm decaffeinated beverage. Drinking a hot tea provides the same psychological effect as drinking hot coffee.

Eat healthy, nourishing, non-processed foods and take a good vitamin supplement. Remember, the 200+ toxins in cigarette smoke have helped deplete the body of vitamins. Five cigarettes can deplete all the vitamin C in the body! By eating a healthy diet, you will recover your health more quickly.

In my preferred embodiment, the smoker is educated to do this for at least the first week, preferably for the first 21 days, after stopping smoking:

Eat 3 meals a day, including breakfast

Have protein and complex carbohydrates with each meal

Avoid sugar

Drink 8 glasses of non-caloric liquids a day—drink water with lemon, seltzer, herbal tea, etc.

Keep a pitcher of water on your desk and you'll easily drink 8 glasses a day

Between meals, drink fruit juices or eat a piece of fruit

Eat lots of fruits, vegetables and salads

As soon as you finish eating, leave the table and go brush your teeth

Use mouthwash whenever possible

In my preferred embodiment, the smoker is admonished: to not skip any meals (and never miss breakfast); to limit refined-sugar intake (and read packaging labels); to avoid beverages with caffeine (tea, colas, coffee, hot chocolate); and, if you must have them, drink tea or coffee out of a juice glass using a straw; and NO alcohol.

We described above the change in blood sugar levels caused by smoking and the physical and emotional response it has on the body. If your blood sugar level gets low, you will either crave a cigarette or something sweet. In either case, it will boost your blood sugar level for 10 to 20 minutes and then cause a crash, triggering another urge for a cigarette or a sweet. By eating 3 meals a day, you will tend to have a stable blood sugar level, and this minimizes cigarette and eating urges. Eating protein with carbohydrates at breakfast sets the stage for stable blood sugar levels all through the day. Protein with complex carbohydrates stabilizes the blood sugar.

I have also found it useful to teach persons quitting smoking to carry a nonfood item such as a swizzle stick or a low calorie food such as celery or carrot sticks. Use these to gratify any oral habit that has been developed by the conditioned response of putting your hand to your mouth 250 times a day, as if you were a one pack a day smoker.

By providing the smoker with this kind of educational program, the smoker is able to consciously and analytically understand their need to smoke and to approach the decision to smoke, or to not smoke, in an analytical, dispassionate manner.

Hypnosis. In addition to the conscious, analytical mind, one can aid the stop-smoking process by using the subconscious mind. In my invention, it is important to use both the conscious mind—via the educational program discussed above—and the unconscious mind, with hypnosis.

The subconscious mind dominates your thinking and behaviors. It is programmed using repetition and the subconscious mind basically behaves for two reasons. It tries to take you towards pleasure and it wants you to stay away from pain. For example, when you have a cup of coffee, you grab a cigarette; you get into a car, you grab a cigarette; you get stuck at a light, you grab a cigarette; you get a break at work, you grab a cigarette; you have a cocktail, you grab a cigarette. If you do not experience these triggers, you may very often go many hours without having a cigarette. It is important that you identify these scenes so we can then break the connection of the cigarettes to the scenes.

With hypnosis, the subconscious mind no longer aids the body to smoke more often, but rather aids the body to stop smoking, during precisely those periods when a smoker is accustomed to having a cigarette. Instead of the subconscious making the body scream for nicotine after a meal, or with coffee or alcohol, the subconscious will help the smoker remain calm and pain free.

When used to stop smoking, I have found that in my preferred embodiment, the hypnosis focuses on interrupting "conditioned responses" generally, and specifically, on interrupting the response to smoke. Conditioned responses are actions (e.g., reaching for a cigarette) motivated not by a consciously-perceived need, but rather by unconscious habit.

Is smoking more of a physical or more of a psychological addiction? For example, how many times have you gone two, three or four hours without even smoking one cigarette and then in another hour you may smoke four, five or six cigarettes? Why is that? It is because certain events, or certain times of the day can trigger you to smoke a cigarette. Therefore, it is necessary to break these unconscious connections, and such breakage occurs, I found, most efficiently using unconscious means—hypnosis.

In my preferred embodiment of my invention, the hypnosis is done in-person and is reinforced later with prerecorded media such as audio-tapes.

Hypnosis techniques are known in the art. In my preferred embodiment, I prefer the in-person hypnosis to follow a six-step protocol. The six steps are (1) neuro-linguistic programming, (2) physical positioning, (3) progressive relaxation, (4) occupying the critical/analytical factor, (5) a process of suggestion, and (6) changing the language of the subconscious.

(1) Neuro-linguistic programming is a technique known in the art. It is described in detail in the following works written since the 1960's.

The Structure of Magic, Vol.1—Richard Bandler/John Grinder

The Structure of Magic, Vol.2—Grinder/Bandler

Patterns of Hypnotic Techniques of M. H. Erickson, Vol.1 Bandler/Grinder

Patterns of Hypnotic Techniques of M. H. Erickson, Vol.2 Grinder/Bandler

Frogs Into Princes—Bandler/Grinder

Tranceformations—Grinder/Bandler

Using Your Brain for a Change—Richard Bandler
Time for a Change—Richard Bandler
Persuasion Engineering—Richard Bandler/John La Valle
The Adventures of Anybody—Richard Bandler
Science and Sanity—Alfred Korzybski
Uncommon Therapy—The Psychiatric Techniques of Erickson—Jay Haley
Training Trances—John Overdurf/Julie Silverthorn
My Voice Will Go With You—Sidney Rosen These are incorporated herein by reference.

(2) Physical positioning is important, to maintain the subject in a state which is both relaxed, yet not sleep-prone.

(3) Physical Positioning and Progressive Relaxation follow the methods known in the art, instructing the subject to progressively relax each part of their body. This can be done with instructions to, for example, physically perform some act, or to mentally visualize some relaxing phenomenon.

(4) Occupying the critical/analytical factor is accomplished in my preferred embodiment by having the subject perform certain tasks which both require some conscious attention, but also are not so difficult or complex as to absorb the subject's entire mental capacity.

(5) The process of suggestion is important to repeat for an effective period of time—usually at least daily for about twenty one days. This time may, however, be less when the subject is relaxed, or is in a highly-emotional state.

(6) The last step is changing the language of the subconscious. This is done by repeating a desired message—e.g., "I am free from smoking"—often enough that the desired message replaces an undesired message in the subconscious mind. For example, one technique is to get friends, coworkers, and family members to help you, by asking them to congratulate you for not smoking. The best way to accomplish this is to stick your hand out to a friend or family member, asking that person to shake your hand and congratulate you for being a nonsmoker. When that person congratulates you, it is a positive reinforcement. The (former) smoker benefits from this positive feedback, and from knowing that they are doing well in stopping smoking.

In another technique I found successful, smoking is described as like having a best friend. Psychologically, the cigarette is the support that a friend gives you. Imagine having your best friend there for you and then losing him or her. You would not feel very good losing your best friend. However, if you discover that your best friend was abusing your children, most likely you would not feel the same about losing your best friend. You would still have some sort of attachment, but now you would be able to reason your way out of not having this person as a friend. In my preferred embodiment, the educational program teaches smokers to look at smoking in the same way.

In my preferred embodiment of my invention, hypnosis is also administered by listening to a prerecorded audio script which provides stop-smoking messages and positive feedback for not smoking. Such audio tapes are commercially available. In my preferred embodiment, I use an audio tape titled "Smoking Cessation," published by Vitamerica, Inc. Cedar Knolls, N.J., www.vitamerica.com, to be listened to once every day for an effective length of time, generally about twenty-one days.

Dietary Substances. The third element of my invention is using proper dietary substances. These address the physiological needs of people breaking their physical addiction to nicotine. Further, one of the biggest fears of smokers is that, in stopping smoking, they will gain excess weight. Thus, in my preferred embodiment, in addition to the dietary substances that support normal form and function while recovering from a smoking addiction, one also uses dietary substances that support normal form and function for those seeking weight-loss or to reduce weight gain. In my preferred embodiment, I recommend CIGSATION™ and TRIM SPECIFICS™, dietary supplements by Vitamerica, Inc., Cedar Knolls, N.J., www.vitamerica.com.

To aid the reader's understanding, I will discuss first the biological basis of the smoking addiction. I will then discuss the dietary substances and the diet modifications I have found effective to combat the physical smoking addiction—the addiction to nicotine. Finally, I will discuss dietary substances to control weight gain.

What causes the addiction to nicotine? The nervous system is divided into two anatomical divisions. The first is the central nervous system, which is composed of the brain and spinal cord. The second is the peripheral nervous system, which includes neurons located outside the brain and spinal cord, which includes any nerves that enter or leave the central nervous system. The peripheral nervous system can be further divided into the efferent division, whose neurons carry signals away from the brain and spinal cord to the peripheral tissues, and the afferent division, whose neurons bring information from the periphery to the central nervous system.

Nerve impulses are transmitted along a path of cells called neurons. The neurons form a knot-like mass called ganglia. These neurons are connected by a series of bridges. The bridge is called a synapse. In order to dross the bridge, a neurotransmitter is required. Before the nerve impulses reach the relay station or bridge, they are referred to a pre-ganglionic neurons. After crossing the synapse, they are referred to as post-ganglionic neurons. The basic neurotransmitters of the autonomic nervous system are acetylcholine and epinephrine. Acetylcholine mediates the transmission of nerve impulses across autonomic ganglia in both the sympathetic and parasympathetic nervous systems.

Nicotine Receptors. These receptors, in addition to binding acetylcholine, also recognize nicotine. Nicotine initially stimulates and then blocks the receptor. There is a competitive inhibition taking place. In lay terms, the receptor has a greater affinity for nicotine than for acetylcholine. At the same time, nicotine increases the level of the neurotransmitter dopamine in a particular brain pathway which associates a molecular link between nicotine addiction and this pleasure producing pathway. This is why nicotine causes such as strong physiological addiction. Recently, scientists at Yale and at the Pasteur Institute in Paris have found that the beta 2 sub unit of a known nicotine receptor in the brain is a critical component in nicotine addiction.

To combat this nicotine addiction, it is useful to use lobelia. *Lobelia inflata* (also known as Indian Tobacco) is a plant. This plant contains three nicotine-like ingredients : 1) lobeline, 2) lobelanidine, and 3) lobelanine. On close inspection of these three ingredients one can notice that all are symmetrical molecules. In other words, if you cut them each in half, each half is the same. The only exception is with lobeline, which has a slight difference on one side of the molecule. I refer to each of these three compounds, their analogs, and derivatives, as "lobelia." After explaining some basic physiology, you will see why lobelia is important.

Nicotine causes an increase in blood pressure, increases intestinal motility, stimulates the central nervous system, has an anti diuretic effect (ability to retain water), affects heart rate, affects respiration, is highly soluble and crosses the blood-brain barrier, produces some euphoria (feeling of well being), arousal, relaxation, and it improves attention, and crosses the placenta membrane and is secreted in the milk of

lactating women. The chronic effects of Nicotine include nasopharyngeal and bronchial irritation, lung cancer, cardiac irregularities, stimulated salivary secretion, and reduction of gastric acidity.

Let us now consider the structural formulas for the active constituents in lobelia. Because of their basically symmetrical structure, it appears that they have an advantage in competing with nicotine at the effector cell site. It is postulated that these components can attach themselves to the cell site from either side of the molecule and perhaps crowd out the nicotine. Later, after the nicotine is eliminated from the system, lobeline will replace nicotine at the effector cell site. While nicotine is rapidly eliminated from the body within 16–24 hours, the withdrawal symptoms can last for several weeks to several months, depending upon the individual.

Lobelia's action in the body mimics that of nicotine, but does not have the physiological dependence of nicotine. Lobelia exhibits a cross tolerance with nicotine, is one of the most useful systemic relaxants, has a relaxation effect on the central nervous system, has a relaxing action on the autonomic nervous system, has a general relaxing action on neuromuscular action, is a powerful respiratory stimulant, equalizes circulation and relieves vascular tension, provides a truly holistic action with a combination of stimulation and relaxation, and also provides the holistic action of a general relaxant with diffusive stimulation.

Recently, scientists in Japan have discovered an antidepressant component in the leaves of *lobelia inflata*. This probably explains why individuals feel better when taking lobelia.

Given this physiology, the physiologic needs of a smoker can be addressed using lobelia. In addition to lobelia, I have found that other herbal substances are useful as dietary substances. Thus, in my preferred embodiment, lobelia is used along with wood betony, fennel seed and licorice root and several other herbs. In addition to these vitamin-type nutritional supplements, in my invention one needs lobelia. Lobelia is also known as Indian tobacco or wild tobacco and is native to North America. It includes three components significant here: lobeline, lobelanidine and lobelanine. It is pharmacologically similar to nicotine, but does not have nicotine's physiological dependency.

In my preferred embodiment of my invention, I have found it beneficial to include certain other supplements derived from plants and herbs. Each the individual ingredients improves the function of lobelia alone, as each provides a specific function to enhance the efficacy of the product.

Wood Betony. Wood betony is used for its sedative and bitter properties. Its anti-hypertensive properties relieve nervous tension and dilate blood vessels, thus producing a calming effect. Wood betony can relieve headaches normally associated with nicotine withdrawal. Its bitter tonic properties also aid in nicotine withdrawal.

Fennel Seed. Fennel seed has been recognized to have carminative and stimulant properties. It has been reported to have a spasmolytic effect on smooth muscles. As a result, it can be used for dyspeptic discomfort, gastrointestinal discomforts and congestion of the upper respiratory tract. Since chain smokers normally have a smoker's cough resulting in congestion of the lungs, fennel seed can aid in treating that congestion. One of the constituents from the volatile oil expressed from fennel is anethol. Anethol has been shown experimentally to reduce secretions of the upper respiratory tract (i.e., lungs).

Licorice Root. The major active ingredient in licorice root is glycyrrhizin. The glycyrrhizin is responsible for a vasopressor response, which is similar to that occurring in nicotine. However, while it mimics that response, it also exhibits anti-inflammatory and an antitussive effects that is comparable to codeine in potency. This is due to the derivative 18 Beta-glycyrrhetinic acid which prevents smoker's cough. In addition, the flavonoids in licorice root have recently been shown to have strong antioxidant and anti-hepatotoxic activities. These activities will help cleanse the body of the free radicals and other toxic substances generated from smoking. Licorice extracts are often used in anti-smoking preparations as a flavoring agent to mask bitter nauseous or other undesirable tastes from other components of the preparation. Licorice can also be used to treat stomach irritation arising from nicotine usage.

In addition to the foregoing, I have found it useful to use also blue cohosh, black walnut husk, chamomile flower, gotu kola leaf extract, kava kava root, peppermint, sarsaparilla root, slippery elm bark, valerian root, bayberry fruit, myrrh, passion flower, ginger root and eucalyptus oil. Thus, in my preferred embodiment, I use each of these, for the following reasons.

Blue Cohosh. It has demonstrated anti-inflammatory activity in animals. Blue cohosh can be used for nervous disorders.

Black Walnut Husk. Black walnut husk is a blood cleanser and oxidizer. It has been shown to be useful in lung disease and has strong anti-fungal and antibacterial properties. It is a rich dietary source of protein, iodine, chromium, potassium, manganese, vitamin A and the powerful antioxidant vitamin C.

Chamomile Flower. Chamomile flower has essential oils that contain a variety of glycosides, and other important constituents and chemically related compounds. Several of the therapeutic constituents of the volatile oil are chamazulene and alpha bisabolol oxide A. Chamazulene has demonstrated anti-inflammatory activity, pain relieving, wound healing, antispasmodic and anti-microbial properties. Alpha bisabolol has anti-inflammatory, anti-microbial and anti-peptic activities. Matricin has been found to have a sufficiently stronger anti-inflammatory effect than chamazulene.

Gotu Kola Leaf Extract. The gotu kola leaves contain properties that have been shown to accelerate wound healing, improve memory, relieve fatigue and stress, increase mental acuity and improve behavioral patterns. This produces a calming effect within the body, thereby relieving the stress associated with nicotine withdrawal symptoms.

Kava Kava Root. The active ingredients in kava kava root are a group of compounds known as the kavalactones. They are recognized for their biological activity as a sedative, anti-convulsive and tonic. Additional constituents in kava kava root have demonstrated muscle relaxant activity and have been used for their ability to combat nervous anxiety and unrest. Kava kava also has expectorant properties. This allows the heavy smoker to expectorate residual mucus from the lungs.

Peppermint. Peppermint yields a volatile oil that is composed mainly of menthol. Menthol has long been recognized as a cooling agent in topical preparations. Also present are many other ingredients, some of which have been characterized to have biological activity. One such constituent is bisabolene, which has demonstrated to have anti-inflammatory activity. Other constituents in peppermint include flavonoids such as hesperetin and rutin. Also present are tocopherols, carotenoids, choline and azulenes. Azulene isolated from peppermint demonstrated anti-inflammatory and antinuclear effects in experimental animals. Peppermint

oil is extensively used as a flavoring agent, carminative, antiseptic and local anesthetic in cold, cough and other preparations. Peppermint and their oils have been used in traditional medicine as a stomachic, stimulant, antiseptic, local anesthetic and antispasmodic in treating indigestion, sore throat, nausea, diarrhea and colds.

Sarsaparilla Root. The major component of sarsaparilla is a variety of steroids which include sarsasapogenin, smilagenin, sitosterol, stigmasterol and pollinastanol, and their glycosides (saponins) including sarsasaponin (parillin), smilasaponin (smilacin), sarsaparilloside and sitosterol glucoside. Sarsaparilla is reported to have hepatoprotective, diuretic and anti-inflammatory activity.

Slippery Elm Bark. The principal constituent of slippery elm bark is mucilage. The mucilage has demulcent (soothing) and nutritive properties. It can sometimes be used to soothe irritated lungs.

Valerian Root. Valerian root has a variety of constituents but the major one, valerenic acid, produces a nerving or sedative effect. Valerian has CNS depressant activities. As a result, in states of agitation normally witnessed by smokers during withdrawal, this will have a calming effect. It has also been shown that in conditions of fatigue, the herb has demonstrated stimulating properties.

Bayberry Fruit. Bayberry fruit has been recognized to have a tonic effect.

Myrrh. Myrrh is reported to have astringent effects on mucus membranes. It is often used as a flavor component to mask bitter ingredients. It has also been used as a stimulant and expectorant. The expectorant properties will help the smoker remove mucus and phlegm from the lungs.

Passion Flower. Passion flower contains indole alkaloids, flavonoids and steroids. The indole alkaloids and flavonoids have tranquilizing effects. Anxiolytic and hypotensive activity has also been reported.

Ginger Root. Ginger root is used to combat nausea and vomiting, which may accompany nicotine withdrawal.

Eucalyptus Leaf Oil. The leaves contain 0.05 to 3.5% oil. The oil consists mostly of eucalyptol (1, 8-cineole). It is used in an anti-smoking formula as an expectorant to help remove mucus from the lungs.

In my preferred embodiment of my invention, these dietary substances are used as found in CIGSATION™ 100% Natural Cigarette Replacement System, commercially available from Vitamerica, Inc., Cedar Knolls, N.J. 07927, www.vitamerica.com. Each of these dietary substances adds to the benefit obtained from using lobelia alone.

In addition to addressing the physical nicotine addiction, I find it useful to address the smoker's fear of excessive weight gain, by using a "weight control product," a drug or dietary substances useful in controlling unnatural weight gain. Such dietary substances include chromium, choline, inositol, vanadium, gynema sylvestre, lecithin, vitamin B6, ginseng, zinc, mahuang, kola nut extract, spirulina, and methionine. Several of these are known physiological stimulants, which increase thermogenesis in the body and thus promote expending calories. I will discuss each in turn, and its usefulness in a weight-control product.

Chromium. What is chromium? It's the mineral that no body can afford to be without. Like iron, copper and zinc, chromium is one of the 16 essential trace minerals the body needs to keep healthy and fit. And for people who are overweight and out of shape, chromium may be the most precious mineral of all. In its biologically active form, it helps insulin to metabolize fat, convert protein into muscle, and convert sugar into energy. Chromium-activated insulin actually increases almost twenty times the amount of glucose available for energy production, optimizing energy output so that you feel healthy and alive.

Chromium is the "master" nutrient for controlling blood sugar. It helps overcome sugar cravings, which is a problem with many overweight people. It also plays an important role in controlling blood lipids, lowering harmful LDL cholesterol, and increasing beneficial HDL cholesterol.

Research shows that a chromium deficiency may be a widespread problem. Many people, such as athletes, diabetics, mothers and the elderly, are at especially high risk. A lack of chromium can impair insulin function, thereby inhibiting protein synthesis and energy production. More seriously, it can even lead to type II diabetes and heart disease.

In my preferred embodiment, the chromium is a form of chromium commercially available under the trade name CHROMIUM CHELAVITE™, available from Vitamerica, Inc. of Cedar Knolls, N.J.

The most biologically active form of chromium, the true GTF chromium, is the basis for the molecular structure of CHROMIUM CHELAVITE™. Studies on CHROMIUM CHELAVITE™ at a leading Utah university have shown that this form of chromium is clearly superior to both chromium picolinate and chromium polynicotinate in absorb ability. It had an absorption rate that was 53% greater than for chromium picolinate and 91% greater than that observed for chromium polynicotinate.

Choline. Choline is one of the most beneficial nutritional supplements. Technically, it is not a vitamin, even though it is essential for human life. There are three major functions of choline among humans. It is needed for building cell structure, it prevents or minimizes unhealthy fat deposits in the liver, and it acts as a precursor to acetylcholine. Acetylcholine is a neurotransmitter in the brain which is responsible for nerve impulses, memory, learning, mood elevation and depression control.

Choline has a very positive effect on the health of the liver. It is a lipotropic agent (fat eliminator) that can cut away fats in the liver to be used instead of energy. Choline aids in weight loss by facilitating Growth Hormone (GH) releasers, controlling cholesterol, and helping control the appetite. It also helps reduce the "gut transit time", the amount of time it takes food to move through the intestines. In addition to helping speed food through the system, choline also plays an important role in the body's ability to metabolize fat and cholesterol.

Inositol. Inositol is a member of the B complex of vitamins. It provides a calming effect, nourishes brain cells, helps reduce cholesterol, slows artery hardening, prevents eczema, and is needed for hair growth and metabolism. It is found in high concentrations in the brain, and serves as a brain cell membrane stabilizer. Inositol also helps in lecithin formation, and aids the body in the metabolism of fat and cholesterol.

Vanadium. A trace mineral like chromium, vanadium is essential for cellular activity and for the formation of bones and teeth. It also inhibits the synthesis of cholesterol and lowers certain forms of high blood pressure. It works remarkably well as a powerful insulin mimic and has been shown to normalize blood sugar levels, even in diabetics.

Gynema Sylvestre. This tropical herb is beginning to receive much attention due to impressive results in recent studies. Gynema Sylvestre appears to have a positive effect in lowering blood sugar levels, especially in diabetics. Research also suggests that it can help curb sugar absorption.

Lecithin. Lecithin is part of every single cell in the body, but has its greatest concentration in the brain. About 17–20%

of the brain is made up from lecithin. Lecithin is an emulsifier. It is used in the manufacture of chocolate, because it keeps it liquid and it keeps it moving. Lecithin does the same thing for the fat in the human body; it keeps it moving, right out of the body.

Lecithin is a natural diuretic and an effective cholesterol reducer. It helps prevent the buildup of cholesterol on arterial walls, thus improving the circulation of the blood. One study that examined 900 men for atherosclerosis (fat deposits in the arteries) showed that those with more than 36% lecithin in the blood had no atherosclerosis. Those with less than 34% showed evidence of the disease.

Lecithin is also the source of two of the hardest to find B-Complex relatives, choline and inositol. A major function of lecithin is to supply choline in the diet. Choline (see entry) has the function of breaking down fat deposits in the body. Our bodies do not manufacture enough choline. Therefore, we must rely upon our food and supplements such as lecithin to make sure that we get enough.

Vitamin B6. Vitamin B6 aids in more bodily functions than any other single nutrient. It facilitates the body's use of carbohydrates, proteins and fats. It promotes mental performance by aiding in the transport of amino acids, which are used by the brain to increase mental energy and memory. It also promotes the transport of choline, and aids in the breakdown of glycogen, the primary fuel for the brain.

Ginseng. For centuries, the Chinese have testified to the beneficial effects of Ginseng on longevity. Ginseng provides stimulation to the entire body, helping to overcome stress and fatigue. Ginseng can regulate and normalize blood pressure and blood sugar levels. It has been called a cure-all and has also been claimed to be a mild sexual stimulant. Over all, Ginseng has a phenomenal effect on the body's energy level.

Zinc. Zinc is another important trace mineral that is used by more than 200 enzymes to keep the body's major metabolic systems going strong. In addition to its role in metabolism, zinc is a potent antioxidant, profoundly important in enhancing the immune system, stimulating cellular growth, reducing excess levels of damaging free radicals, and improving general health.

Mahuang. Mahuang, also known as ephedra, contains a potent alkaloid, ephedrine. This natural stimulant increases the basal metabolic rate, which helps to burn calories more effectively. It has also been used as a remedy for kidney and bladder problems, as well as for colds, asthma, and hay fever.

Kola Nut Extract. This is a natural stimulant that increases energy and stamina. It has been found to be very useful in preventing fatigue. Kola Nut Extract also acts as a tonic agent for the heart, and it is sometimes useful in relieving pain, neuralgia, and headache.

Spirulina. This famed blue-green algae contains concentrations of nutrients unlike any other single grain, plant or herb. This super nutrient is a naturally digestible food that aids in protecting the immune system, in cholesterol reduction and in mineral absorption. It also helps to cleanse and heal, while also curbing the appetite.

Methionine. Methionine is an amino acid that assists the gall bladder function by helping to synthesize bile salts. It is a lipotropic substance that prevents the deposits of and cohesion of fats in the liver. It is also reported to be a growth hormone releaser.

It serves as an antioxidant in the brain. It helps prevent the buildup of heavy metals and plays an important and essential role in the production of the brain neurotransmitter choline. Methionine is not found in the body. Therefore, it must be gotten via food and supplementation. It is also a good source of sulfur, and its therapeutic lipotropic effects help to eliminate fatty substances from the body.

Each of these dietary substances can be found in TRIM SPECIFICS™, available from Vitamerica, Cedar Knolls, N.J., www.vitamerica.com.

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, utilize the present invention to is fullest extent. The examples I discuss here are included as the preferred embodiment of my invention, and not to further qualify the description.

I claim:

1. A method for helping a tobacco smoker to stop smoking, said method comprising the steps of:

(A) providing to a tobacco smoker a non-conditioning, educational program to educate said tobacco smoker's conscious mind, said educational program including education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) providing to said tobacco smoker at least one hypnosis program to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) providing to said tobacco smoker an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco,

such that said tobacco smoker can be helped to stop smoking.

2. The method of claim 1, where said hypnosis program comprises prerecorded media useable by said tobacco smoker when alone.

3. A product to aid a tobacco smoker in ceasing to smoke tobacco, said product comprising:

(A) means for educating said tobacco smoker's conscious mind, said educational program including non-conditioning education both on the disadvantages of smoking and on conscious techniques to stop smoking,

(B) means for hypnosis to train said tobacco smoker's subconscious mind to discourage said tobacco smoker from performing smoking behavior, and

(C) an anti-smoking drug in an amount effective to aid in the reduction or cessation of said tobacco smoker's craving to smoke tobacco.

4. The product of claim 3, where said means for hypnosis comprises prerecorded media useable by said tobacco smoker when alone.

5. The method of claim 1, further comprising the step of: (D) providing to said tobacco smoker, at least one weight-control product, in an amount effective to aid in weight control.

6. The method of claim 5, where the weight control product includes at least one stimulant in an amount effective to aid in weight control.

7. The product of claim 3, further comprising: (D) at least one weight-control product in an amount effective to aid in weight control.

8. The product of claim 7, where the weight control product includes at least one stimulant in an amount effective to aid weight control.

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